Public Health
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PHLS Annual Report 1982/3

PHLS
Annual Report

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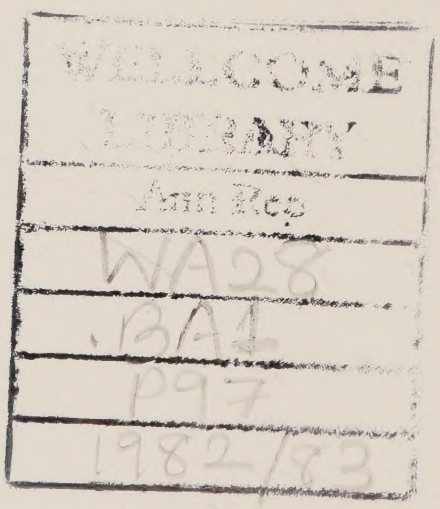
Front cover illustration: *Public Health Microbiology 100 years ago*

In 1882/3 the immunization of domestic animals against anthrax became a commonplace following the first successful experiment by Louis Pasteur in May 1881. The illustration shows Dr Cartaz, an associate of Pasteur, inoculating a sheep, from an article in *La Nature*, Paris, of 11 February 1882. A report in *The Lancet* of 13 January 1883 stated: 'The number of sheep which have been vaccinated more than a year is now 79,520 [in the department of Eure-et-Loire] . . . . Of the innocuity of the process of inoculation . . ., a striking proof was mentioned by M. Pasteur, in communicating . . . to the Academie des Sciences. During the preceding six weeks no less than 13,000 sheep, 3500 oxen, and 20 horses had been inoculated, and of the total of 16,520 animals not one had died.' [Illustration supplied by Ann Ronan Picture Library, Taunton, Somerset.]



Typeset by Devon Print Group, Exeter.

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Introduction

Further changes have been made in the format of the Report this year to modify the tendency towards a "telephone directory" style in recording the work of the Service. A statement by the Chairman of the Board is included for the first time, marking the closer involvement of the Board in guiding the affairs of the PHLS. In his statement Dr Gordon Smith addresses some of the principal problems currently facing the Board in operating the Service. Another change is the omission of the detailed list of publications by members of the PHLS (this will be published separately and may be had on application to the Librarian at the Central Public Health Laboratory, Colindale), and the substitution instead of a summary analysis of the publications by numbers and main topics (see Table 2, page 25).

The report of the Director of the Service is presented under three main headings – routine, research and financial and administrative aspects. In an organization as varied and complex as the PHLS, to draw a distinction between those areas of work which are routine and those which are research is somewhat artificial, a point returned to later, on page 15. Finance and administration likewise impinge on both. The aim of tripartite presentation is to offer a more readily assimilable picture of the activities of the various parts of the Service than might otherwise be possible.

The section on the routine work of the Service makes plain that this comprises more than it is customarily thought to be – the examination of various kinds of specimens submitted to the regional, area and reference laboratories. The routine nature of other activities needs to be recognized, such as the surveillance of communicable disease and of immunization programmes, the production of biological materials and the issue of cultures and reagents. Appropriately reference is also made in this section to the giving of advice, for it forms a significant element in routine work throughout a Service which is, and always has been, largely consultative.

The continuing rise in the number of specimens examined in the regional and area laboratories, with a "knock on" effect on the reference laboratories, is only a partial measure of the increased demand for laboratory services in medical microbiology, for the figures take no account of the specimens whose examination has had to be declined. With finite – and diminishing – resources at their disposal, laboratory directors are increasingly obliged to operate a form of microbiological "triage", or priority

assessment, of the specimens and tests requested so as to ensure that their laboratory resources are deployed to the best advantage for the main purposes of the PHLS, i.e. the diagnosis, prevention and control of communicable disease. Triage is, however, time consuming, for to be acceptable it requires personal explanation and discussion with the user, usually by a medical member of the laboratory staff since there may be clinical implications.

Mention is made in the section on research of the difficulty in which this area of activity is placed during times of financial stringency when priority has to be given to meeting the demands of routine work. To press these demands to the limit and restrict research entirely would soon lead to deterioration in the quality of the routine service; if laboratory techniques are to remain efficient, they must be subject to continuous evaluation and development. Present financial circumstances call for fine judgement on the part of laboratory directors in gauging the extent to which they can justifiably sustain some research activities from the overall allocation of resources made to their laboratories. In regional and area laboratories, and to a certain extent in the reference laboratories also, the choice of projects under these circumstances tends to be confined to those which can be proceeded with when the pressure of routine work eases and put aside when it mounts again.

The range of topics on which research is currently conducted has widened considerably since the PHLS Centre for Applied Microbiology and Research (CAMR) became part of the Service in 1979; this is illustrated by the variety of work described in the section on research and which only represents a selection of those projects in progress. Because of the obligation of the PHLS Board to the Secretary of State to offset as much of the expenditure on CAMR as is reasonably practicable, the staff engaged in research at Porton have to be alert to the commercial potential of their work, an awareness which is beginning to manifest itself in other parts of the PHLS as commercial firms increasingly show interest in PHLS research and development. To enable discussion to proceed between the staff concerned and representatives of industrial concerns, a standard form of confidentiality agreement has been drawn up and brought into use.

The section on finance and administration illustrates how the Board's finances are allocated and how they have been affected by Government policy; at the same time it shows the considerable increase in the income generated by the Board. It also sets out the progress of the Board's capital schemes, including the long awaited New Colindale which is expected to be handed over by the contractors, Mowlem-Andrews-Weatherfoil, in the autumn of 1984. An account is also given of the way in which equipment for purchase by the Service is evaluated and of developments in the use of computers in the PHLS both for scientific and administrative purposes.

The sections of the Report which follow represent a distillate, and in the case of CAMR and the Central Public Health Laboratory, a re-distillate, of

information supplied by laboratory directors, administrative staff and other colleagues. Their help is gratefully acknowledged, as is also the advice and assistance of the Publications Editor in preparing the Report for publication.

The Report is supplemented with six short articles by individual contributors. These "special topics" have been chosen for their intrinsic interest and as examples of the varied ways in which the Service meets its overall objectives.

The first, which deals with streptococcal infections in establishments for young offenders, shows how relevant is the national scale of organization of the PHLS for investigating an infection which is dispersed throughout the country by the movement of inmates from one establishment to another.

The second is an example of the persistence with which the Director of a joint PHLS/NHS laboratory sought out the environmental source of a rare and fatal infection in a child which had been diagnosed in his laboratory as part of the microbiological service given to its associated hospitals.

The third shows how a commonplace, although imperfectly understood, infection of humans and animals, in the special circumstances of cardiac transplantation can cause the death of patients undergoing this advanced surgery, and calls for more information to be gathered about its epidemiology.

The fourth demonstrates how a laboratory, through its services to communities outside hospital, in this instance to a boarding school, has been able to develop a local "test-bed" in which to evaluate by clinical and detailed laboratory studies the actual – and remarkably limited – effect of influenza vaccination.

The fifth represents the application of microbiology to the solution of a problem in another discipline, chemical pathology, and is a model of the kinds of development in the field of health care expected of CAMR in the future.

The last demonstrates how, through the combined efforts of many different parts of the Service in investigating an unusual and widespread outbreak of salmonella infection conveyed by imported chocolate, many cases of a communicable disease were prevented, with consequent saving of public expenditure – an exemplary justification of the preventive role of the PHLS in the country's health services.

The PHLS: What it is and What it Does

LEGISLATIVE BACKGROUND

In 1945 the Government decided, in view of the outstanding success and growing dependence on the wartime Emergency Public Health Laboratory Service, to put it on a permanent footing and the Medical Research Council (MRC) agreed with the Ministry of Health to continue their administration of it for five years. Statutory authority was given by Section 17 of the NHS Act 1946 to the Minister to provide a bacteriological service for the control of the spread of infectious diseases.

The PHLS Act 1960 established and incorporated a new PHLS Board as a statutory body, capable of acting in its own right as an agent for the Minister of Health. The Act also transferred the staff from the employment of the MRC to that of the Board and transferred property from the Council to the Ministry.

The NHS Act 1977 (Schedule 3) incorporated the PHLS Board. Part I dealt with the formal consititution of the Board and Part II with staffing and financial provisions. The PHLS Act 1979 gave responsibility to the Board for the former Microbiological Research Establishment of the Ministry of Defence at Porton Down and extended the Board's powers to carry out "such other activities as in the Secretary of State's opinion can be conveniently carried on in conjunction with the Service".

The PHLS is administered by a Statutory Board, closely analogous to a Regional Health Authority or a Special Health Authority. It is an integral part of the National Health Service and has responsibility extending over the whole of England and Wales. The staff receive the same rates of pay as those employed in the NHS, which may only be varied by direction of the Secretary of State, and are required to join the NHS Superannuation Scheme. The Board's staff formally came within the purview of the Health Services Whitley Councils on 1 March 1981. The Board had Management representatives on the PTA and PTB Councils.

STRUCTURE

The PHLS comprises 52 regional and area laboratories distributed throughout England and Wales (see Figure 1), and 23 reference and special

laboratories or units, most of which are grouped in the Central Public Health Laboratory, Colindale, North London (CPHL), or at the PHLS Centre for Applied Microbiology and Research, Porton Down, Wiltshire (CAMR).

Figure 1 Map showing the geographical distribution of PHLS laboratories.

FUNCTIONS

The PHLS operates as a network of centrally co-ordinated laboratories in accordance with its statutory obligations both to provide a microbiological service for the diagnosis, control and prevention of communicable diseases and to develop applications of biotechnology mainly, but not exclusively, in the health field. It carries out these obligations by giving a routine microbiological service to several hospitals, and providing reference facilities that are available nationally. It collates information on the incidence of infection, and when necessary it institutes special enquiries into outbreaks and the epidemiology of infectious disease, although executive responsibility for their control is the statutory responsibility of local authorities. It also undertakes bacteriological surveillance of the quality of food and water for local authorities and others. The PHLS is often called upon to advise central and local government and the hospital service on many aspects of infectious disease. It maintains close contact with veterinary organizations in areas of mutual interest, and collaborates with the World Health Organization and with national laboratory and epidemiological services overseas. Particularly at CAMR there is collaboration with commercial organizations on ways of applying expertise to industrial developments.

ROUTINE DIAGNOSTIC MICROBIOLOGICAL SERVICE

Nearly all of the regional and area laboratories are situated in or are closely associated with hospitals, providing them with their routine clinical microbiological service. They also serve general practitioners, Medical Officers for Environmental Health, other doctors caring for communities and Environmental Health Officers. By means of this continuous sampling the PHLS monitors the infections which bring patients to hospital or which attack them while they are there, as well as becoming aware of the distribution of infectious disease in the community.

REFERENCE AND SPECIAL FACILITIES

Most of the regional and some of the area PHLS laboratories carry out special tests for neighbouring PHLS and NHS laboratories. All PHLS laboratories are available to assist local hospital laboratories in investigating outbreaks of infection, if asked to do so.

Further back-up facilities are provided by the reference laboratories or units which carry out various tests for the PHLS and hospital laboratories throughout the United Kingdom. These tests usually require special expertise, techniques and facilities which it would be uneconomic or impossible to provide more widely. As well as carrying out special tests such as the "fingerprinting" of organisms for epidemiological purposes, reference lab-

oratories conduct research and act as sources of advice on many aspects of the control of communicable disease.

The PHLS laboratories at Colindale and Porton Down develop and produce therapeutic, prophylactic and diagnostic materials for use by the NHS and others, as well as by the Service itself. They also monitor commercially available reagents and provide test material to PHLS and hospital laboratories to enable them to assess the quality of their routine performance. The National Collection of Type Cultures (of bacteria of interest to medicine) is a constituent part of the Central Laboratory at Colindale.

DISEASE SURVEILLANCE AND CONTROL

A special unit, the PHLS Communicable Disease Surveillance Centre, analyses information about the whole range of infectious diseases from the regular reports they receive from the PHLS and hospital laboratories. These data form a continuously changing, up-to-date picture of communicable disease throughout the country. This is published weekly in the *Communicable Disease Report*, which is issued to microbiologists, community physicians and others concerned with disease control, supplementing information available from the statutory notifications and other sources. In addition to gathering information, the Centre co-ordinates the investigation and control of incidents of communicable disease of national importance and of outbreaks involving more than one local authority.

A unique feature of the PHLS is the regular meeting together four or five times each year of the heads of its laboratories to exchange information and discuss technical matters. It is thus enabled, at short notice, to call on the very wide range of knowledge and ability available among its nationally distributed specialist staff. Working parties with appropriate skills can be formed to tackle new problems, as they arise, achieving the highest probability of producing a speedy and useful result. There have been several examples of this system operating in recent years, to the considerable benefit of the community.

The Epidemiological Research Laboratory undertakes surveillance of the effectiveness and safety of many of the immunization programmes in current use, and evaluates new immunization procedures.

RESEARCH

Most PHLS laboratories are engaged in some research, and many regional laboratories, and especially the reference and special laboratories, have extensive research programmes. CAMR in particular has a substantial programme of research and development in the sciences underlying biotechnological processes and their application. The Service has a number of committees which organize collaborative research projects and arrange for the testing of new ideas and methods.

SURVEILLANCE OF FOOD AND DRINK

All regional and area laboratories provide a microbiological service to local authorities for the examination of water, milk and, increasingly, other foodstuffs, including imported foods examined at the port of entry or centre of distribution. Raw foods, in particular meat and poultry, and animal feeds known to spread agents of food poisoning are monitored to trace the origin and transmission of these organisms. Food-poisoning bacteria are studied in relation to their survival or multiplication in foods and preventive measures are suggested in the light of results. Laboratories are often called on to examine foodstuffs in the course of investigating outbreaks of infection and they may be invited to advise manufacturers.

ACCEPTANCE OF SPECIMENS

The material examined in PHLS laboratories comprises "clinical" specimens (throat swabs, blood, faeces, etc.) from persons suspected of suffering from a microbial disease, or of being carriers of pathogenic microbes, and non-clinical ("sanitary") specimens, such as food and water, submitted either as part of an epidemiological investigation or for routine public health surveillance.

Clinical specimens must be submitted by medical practitioners, veterinarians, dentists or those acting directly on their behalf. Clinical specimens are not accepted from other private persons.

Sanitary specimens can be submitted by Medical Officers for Environmental Health and Environmental Health Officers (or members of their staff) acting on behalf of the local authorities. The PHLS is always ready to give advice to food manufacturers and distributors; however, although it may carry out limited microbiological investigations related to the inquiry, it does not ordinarily undertake routine examinations for commercial organizations.

The reference and special laboratories receive only specimens sent from other laboratories. Their services are available to all PHLS, NHS and other official laboratories in the United Kingdom.

Statement by the Chairman of the PHLS Board

It had already become clear by the beginning of 1982 that most of the desirable developments foreshadowed in the Board's plan for the 1980s entitled, optimistically perhaps, "PHLS: The Way Forward", were unachievable within the reduced cash limits currently available to the Board and that, for the medium term at least, further contraction was to be expected. It seemed to me that in order not to lose sight of the objectives which the Board had previously endorsed and to apply its reduced resources most effectively to the discharge of its statutory responsibilities, a searching review of the role and functions of all aspects of the PHLS was called for, and with the agreement of the Board this was begun during the year.

The review is being carried out in two stages. The first consisted in my seeking the confidential opinions of Members of the Board, its Staff Assessors and Senior Officers, and of several representative users of the Service about the strengths and weaknesses of the PHLS and the direction in which it should aim to develop during the remainder of the decade. I personally collated their replies in a paper which the Board discussed and which the Director of the Service subsequently refined as "The Case for the PHLS". This formed a common background against which the four Working Parties, which the Board established as the second stage of its review, were to deliberate. Each was composed of Board Members, members of the Service and outside experts and considered separate areas of PHLS activity: regional and area laboratories, epidemiological services, reference services (including "new technology") and research. By the end of the period covered by this Report, these Strategic Review Working Parties were well advanced on their tasks and showed every prospect of meeting the deadline of reporting to the Board at its meeting in July 1983.

In my view it is only after a thorough and well conducted appraisal of this kind that the Board will be justified in the present financial climate in taking steps to reallocate its scarce resources to new areas of activity. By having carried out its own review beforehand, the Board will also be better placed to respond to the findings of the review of the PHLS which the DHSS is at present conducting on behalf of the Management and Personnel Office of the Treasury.

All this scrutiny coming at different times from different sources for different purposes cannot but have an unsettling effect on the morale of the Service and it is greatly to the credit of the staff that the day to day work of the PHLS has been little affected, if at all. If these various reviews were to be to the benefit of the PHLS, it was essential that all who were called upon to participate in them or to respond to them did so willingly and positively. I am grateful to all who did so, despite the load and irritation it may have imposed on a few of them, and am confident of their future co-operation.

I have not touched on the subject of income-generating activities. This is the province of the Board's Standing Committee for Income Generating Activities (SCIGA) which, under the Chairmanship of Professor M. H. Richmond, FRS, has been given a widened remit to include possibilities for generating income elsewhere in the PHLS in addition to CAMR. In the course of three visits which the Parliamentary Under Secretary of State for Health, Lord Trefgarne, paid during the year to various of our laboratories, he stressed the Government's concern that the Board should do everything in its power, consistent with the maintenance of its statutory objectives, to reduce the net cost of the Service to public funds. The Board is grateful to him for his assistance in this by smoothing some of the obstacles which result from the Treasury rules under which the Board is obliged to operate.

The PHLS cannot expect immunity from the economies being made in public expenditure. The Board sees it as its task to encourage the Service to adapt its activities so as to provide the most effective and efficient service that the reduced financial provision will allow.

I wish to record my thanks for the invaluable help and guidance given by Professor R. A. Shooter and Dr W. O. Williams who retired from the Board on 31 July 1982. They were replaced by Professor Rosalinde Hurley and Dr Ian Gregg. The latter unfortunately had to resign after only one year's service. In addition I welcome two new members on to the Board, Mr D. F. R. Crofton and Mr P. Higham, who bring with them valuable commercial experience. The full list of current Board Members is shown on pages 13–14.

Dr P. G. Mann's period of office as Consultant Medical Microbiologist Staff Assessor to the Board expired during the year. He was succeeded by Dr G. C. Turner, Director of the PHLS Laboratory at Liverpool.

C.E. Gordon Smith

Public Health Laboratory Service Board

Membership of the Board is given at at 31 December 1983.

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Report of the Director of the Service

The Routine Work of the Service

It is convenient to consider the work of the PHLS as falling into two parts, routine and research, but in practice the borderline between the two is imprecise and the distinction is to some extent artificial. It could be held, for example, that the routine activities of the PHLS Centre for Applied Microbiology and Research (CAMR) are those implicit in its name and that its routine work is doing research, although in fact CAMR has several service functions and routine production activities. Equally, the routine investigation of episodes of communicable diseases by the regional and area laboratories, with or without involvement of the reference laboratories or the PHLS Communicable Disease Surveillance Centre (CDSC), may sometimes transcend what might be regarded as normal routine practice because of the particular circumstances and nature of the episode and may lead into scientific studies from which new knowledge accrues. This section of the Report reviews the everyday activities of the PHLS, most of which are prompted by demand.

EXAMINATION OF SPECIMENS BY REGIONAL AND AREA LABORATORIES

The number of microbiological specimens examined in the area and regional laboratories in 1982/3, and their type, is shown in Table 1. For the first time these figures relate to the fiscal rather than the calendar year, to bring them into line with the rest of the Report.

The total of specimens examined in 1982/3 exceeded that for 1981 by 4.4 per cent, maintaining the steady increase of about 4 per cent per annum that has been apparent for some years. Last year evidence was presented which suggested that the number of specimens might have reached a plateau. This has proved to be transitory, as the number received this year in 43 of the 52 area and regional laboratories was greater than in 1981.

PATTERN OF DEMAND

Within the major groups of specimen, the proportion submitted for virological examination increased most markedly, and the number of environ-

Table 1 Specimens examined in regional and area laboratories, 1982/3

Source	Examination	No. of specimens	Totals
Human	For bacteria		
	in urine	1 905 323	
	for tubercle bacilli	161 822	
	for other bacteria and fungi	2 335 150	4 402 295
	For chlamydia and viruses (including by electron microscopy)	246 964	246 964
	Antigen-antibody detection		
	in venereal diseases	420 145	
	in bacterial diseases	109 181	
	in viral and other diseases	953 353	1 482 679
	Antimicrobial assays	27 941	27 941
Animal	Diagnosis of disease	3 983	3 983
Food	For microbial contamination		
	water, milk, cream, ice cream	164 347	
	other foods	40 749	
Other environmental specimens		82 819	287 915
Various reference specimens		82 790	82 790
			6 534 567

mental specimens continued the minor downward trend that has been evident since the early 1970s. Classified by source, 70 per cent of the specimens were from patients in hospital, and 24 per cent were submitted by general practitioners, while 6 per cent were from environmental sources. This represents a small shift in the proportion of specimens received from hospitals in favour of general practice.

Some of the continuing increase in workload reflects a significant concomitant change in hospital activity. For some years, the number of patients passing through NHS hospitals has risen steadily, despite a simultaneous and quite marked fall in the number of hospital beds provided. This has been achieved by reducing the average length of time each patient stays in hospital. The maximum demand for laboratory investigation comes in the early stage of a patient's admission, when diagnoses are being made. For this

reason, with more patients spending less time in hospital, a disproportionately larger number of specimens is generated, to which has to be added the extra examinations which arise in general practice early in the follow up of recently discharged patients. If to this is added the ever increasing complexity of medical diagnosis and treatment, which leads to greater dependence on laboratory data, much of the 4 per cent annual increase in workload is readily explained, and some of it perhaps justified. This is not to say that all laboratory tests requested represent real need. Continuous scrutiny is required if irrelevant work is to be kept to a minimum, but it would be wrong to infer that much of the continuing increase in workload results from unreasoning use of laboratory facilities.

USE OF REFERENCE LABORATORIES

Underpinning the activities of the regional and area laboratories are the services provided by the various reference laboratories of the PHLS. Their specialized knowledge and experience are called upon not only by PHLS laboratories but proportionately more so by the more numerous laboratories outside the PHLS such as NHS, university and other laboratories, including some in the veterinary and industrial fields. Nor are their services limited to England and Wales but are also made available in many cases to the rest of the United Kingdom.

Like the regional and area laboratories their routine activities in the fine identification of microbes, the characterization of aberrant strains and the performance of special tests or tests for uncommon diseases are led by demand which follows a similar trend to that observed in the regional and area laboratories. In addition several reference laboratories are designated by the World Health Organization to act as centres for reference and research and this imposes an additional demand on resources which is only partly offset by the funding received from the Organization. Two examples illustrate the scale of the demand:

(a) A total of 667 "difficult" or unusual strains of bacteria were identified, 388 with computer assistance, in the National Collection of Type Cultures, Colindale.
(b) About 30 000 strains of intestinal pathogenic bacteria – mostly salmonellas (but including typhoid bacilli), shigellas (dysentery bacilli), and *Escherichia coli* – were received for typing by the Division of Enteric Pathogens, Colindale.

SOME COMMON FEATURES

Undifferentiated respiratory illness Among the reports from individual laboratories certain common features stand out. Although the winter of 1982/3 was not accompanied by an epidemic of influenza as judged by the

usual criteria, a significant amount of illness due to this virus was recorded in several widely distributed laboratories. It must be assumed that these cases of influenza were lost among the general mass of respiratory illness that recurs each winter. Much work is needed to disentangle the epidemiology of the many causes of respiratory infection, and it may be that the emphasis of research should change to take account of this.

Newer causes of gastroenteritis The availability of methods for identifying more and more bacterial and viral causes of what until recently was classed as non-specific infectious diarrhoea has allowed the epidemiology of these conditions to be better defined, with the hope of controlling them more effectively. Many laboratories are now in a position to detect bacteria and viruses responsible for gastroenteritis whose existence was unsuspected a few years ago.

Streptococcal infections The potential for serious disease possessed by the haemolytic streptococcus, so well recognized by the previous generation of microbiologists, remains perilously close to the surface. The organism emerges occasionally and capriciously to display its ability to kill suddenly or to cause serious chronic ill-health. Recently the latter type of complication has appeared in a number of the places where young offenders undergo custodial sentences. A study of this problem and its control is being made in collaboration with the Home Office (see pages 43–44).

Hepatitis tests More laboratories are now able to test serum samples for evidence of hepatitis A virus infection. The availability of tests for both hepatitis A and B viruses opens the way to a more complete study of the epidemiology and therefore the better control of individual cases and outbreaks of infectious hepatitis.

Advisory functions The unquantified work of laboratories in fulfilling their role as sources of expert advice on communicable disease and the issue of immunoglobulins and vaccines for their control, as well as for the collection of epidemiological data, goes largely unsung, but should not go unrecorded. Although these activities absorb a good deal of professional energy and time they represent a highly cost-effective way of providing a service that only remains low-key because it is performed so efficiently.

Industrial action in the water industry The effect of industrial action during January and February 1983 on laboratories, like that on the general public, was patchy. Most laboratories experienced an increased call on their services for advice: one director reported a quest for long forgotten boreholes at the local hospital, and for testing; another laboratory examined more water in a month than it normally does in a year. The distribution of the "Guide to the microbiological implications of emergencies in the water

service", prepared by a subcommittee of the Microbiology Working Group of the National Water Council, to all PHLS laboratories as soon as the possible threat to water supplies developed ensured uniformity in the advice they gave. Its recommendations were based on the experience gained during previous periods of industrial action and plant breakdown and were essentially practical in content.

COMMUNICABLE DISEASES 1982/3

There were several outbreaks of infectious disease worthy of mention, although none, fortunately, was disastrous.

Salmonella napoli Between April and August 1982, 272 human isolates of *S. napoli*, an exceptionally high number, were reported. Epidemiological investigation traced the outbreak to imported Italian chocolate; this is described in more detail on pages 52–53.

Diphtheria Two cases of clinical diphtheria occurred in August–September, one in Hampshire and the other in London. An extensive contact tracing exercise followed, involving collection of several hundred nose and throat swabs, immunization and antibiotic prophylaxis of close contacts. Seven symptomless contacts of the two cases were shown to be carrying the same sucrose-fermenting toxin-producing strain of *Corynebacterium diphtheriae* var. *mitis*, and sucrose-fermenting strains, which did not produce diphtheria toxin, were isolated from three other contacts. No connection between the two cases was ever established.

Haverhill fever An outbreak of infection caused by *Streptobacillus moniliformis*, an unusual organism generally associated with "rat-bite fever", affected 234 girls in a boarding school in south-eastern England, approximately a third of the total of about 700 persons at risk. The source of infection was not confirmed microbiologically, but detailed epidemiological investigation showed a significant association between drinking water and the development of illness. Although the school had recently been connected to the mains system, it was possible that the water supply could have been contaminated with water from a spring where rats were seen.

Fish and shellfish Eighty-two incidents of food poisoning from fish and shellfish involving more than 269 cases were reported in 1982, compared with 36 incidents in 1981. These included 29 incidents of scombrotoxin poisoning (mostly from mackerel, canned pilchards and tuna) in which the early stages of bacterial decomposition of the muscle of these varieties of fish are accompanied by the formation of histamine-like substances. There were also seven incidents of gastroenteritis from oysters and cockles due to small round structured viruses, 35 of gastroenteritis of unknown cause (26 from

canned salmon, nine from shellfish), and 14 single incidents of infection by *Vibrio parahaemolyticus*, a cholera-like organism, all of them acquired abroad. In addition to these outbreaks of gastroenteritis, six outbreaks of hepatitis A, affecting at least 172 persons, were attributed to shellfish. Two were associated with fresh cockles from Essex; two with frozen cockles from the Netherlands; two with mussels from Ireland; and one with oysters from Devon.

Milk It is disappointing to have to report that raw milk still accounts for some foodborne infection. All 15 reported outbreaks of milkborne salmonellosis, comprising at least 412 cases, were due to raw milk, as were three of the four milkborne campylobacter outbreaks, involving over 600 cases. The other campylobacter outbreak was caused by pasteurized milk which had become contaminated.

SURVEILLANCE OF INFECTION

Virus infections caused a few minor epidemics during the year. An outbreak of echovirus type 11 – an intestinal virus – in the autumn of 1982 was fortunately not as extensive, nor as serious, as that of 1978. In that year 1488 infections were reported, with 11 deaths among newborn infants; in 1982, there were 475 infections with no neonatal death, although one outbreak occurred in a Special Care Baby Unit. Of the other enteroviruses only coxsackie B4 virus was prominent and caused a small outbreak in which 292 cases were reported.

Of the respiratory infections, respiratory syncytial virus appeared unexpectedly about two and a half months earlier than usual, reaching a peak around Christmas rather than in late February or March. The outbreak was also somewhat larger than usual. Influenza A caused a moderate outbreak in January–March in 1983, which was nevertheless the largest recorded during the past five years; about 80 per cent of the viruses typed belonged to the subtype H3N2, and the rest to H1N1 (the earlier virus related to that causing "swine 'flu").

Mycoplasma pneumoniae, a cause of "atypical" pneumonia, which exhibits cycles of infection extending over about four years, caused an outbreak in 1982 which had started in mid-1981 and reached a peak at the beginning of 1983, before falling off rapidly thereafter. Whooping cough has a similar epidemic cycle, and the 1982 outbreak in England and Wales, the second of some size since vaccination declined in the mid-1970s, began in mid-1981 and continued until mid-1983; altogether about 92 000 cases were notified during this two year period.

Surveillance of other infections showed the following: a moderate-sized outbreak of rubella in 1982; a steady rise in notifications of infective jaundice and laboratory reports of hepatitis A (but not hepatitis B) from 1981 to a peak in the summer of 1982 and then declining; a continuing rise in

reports of infections with pencillin-resistant gonococci, with 1033 cases in 1982; and 138 cases of legionella infection, with a mortality rate of about 12 per cent. There was a history of recent travel abroad in about half the cases.

A surveillance scheme set up by the PHLS Communicable Disease Surveillance Centre for cases of the newly described acquired immune deficiency syndrome (AIDS) collected 14 cases between 1 January 1982 and 31 July 1983, of which 12 were in homosexuals, one was in a haemophiliac who had received an anti-haemophilic blood product (Factor VIII) imported from the USA, and one other was a patient who had no known risk factors.

SURVEILLANCE OF EXOTIC PATHOGENS

Dangerous (category A) pathogens Ninety-two specimens from acutely ill patients suspected of suffering from viral haemorrhagic fever were examined at the Special Pathogens Reference Laboratory (SPRL), CAMR. Lassa virus was isolated from only one patient – a Nigerian woman admitted to Coppetts Wood Hospital in October 1982.

This laboratory also tested 857 sera for antibodies to a range of haemorrhagic fever viruses, 98 from an outbreak in Ghana and 502 from one in Kuwait. Results on the Ghanaian sera were negative but 25 patients in Kuwait showed evidence of infection by Crimean haemorrhagic fever virus.

Other exotic infections Tests at the SPRL for antibodies to various arthropod-borne viruses were made on 1283 specimens. Evidence of infection by Dengue viruses was found in several British tourists who had been exposed while holidaying overseas.

Fifty of 213 sera submitted for testing for rickettsial infections at the SPRL were found to be positive, 39 for the spotted fever group and 11 for the epidemic typhus group, all of the latter probably flea-borne typhus.

Coxiella burneti (Q fever) was grown from the heart valves of two patients with suspected Q fever endocarditis.

SURVEILLANCE OF IMMUNIZATION

Whooping cough (pertussis) Assessment of whooping cough vaccine shows that it confers substantial protection (around 80 per cent) against severe disease, mitigates such attacks as do occur and reduces spread. With current vaccines mild attacks sometimes occur despite vaccination and may result in spread to contacts, especially close household contacts. These two factors have probably been responsible for the rather slow decline of whooping cough notifications despite the widespread use of vaccine.

Comparison of severity of whooping cough based on hospital admissions, complications and deaths in 1974/5 and in subsequent outbreaks suggests

that whooping cough remains a severe disease for young infants and children.

In a study of 10 000 children in Hertfordshire made by the PHLS Epidemiological Research Laboratory, preliminary analysis shows that neurological disorder is no more common in children vaccinated with diphtheria-tetanus-pertussis (DTP) than with diphtheria-tetanus (DT) vaccine. There was no evidence there or in a seven year survey in the North West Thames Region of neurological disorders following vaccination which might substantiate claims that DTP vaccine represents a specific hazard to health. At a time when hazards attributed to pertussis vaccination are widely publicised, reports of reactions to DTP vaccine are likely to be heavily biased.

Rubella (German measles) The impact of the progress of rubella vaccination of schoolgirls and of mothers after childbirth is being assessed by comparing the incidence of rubella infections in women of various ages during their first or subsequent pregnancies. Infants infected in the first 16 weeks of pregnancy will be surveyed for some years to detect late developing defects.

Varicella-zoster The Epidemiological Research Laboratory, with the Manchester regional laboratory, has been following up women who develop chickenpox (varicella) or zoster during pregnancy or after childbirth. Evidence of transmission of varicella-zoster virus from mother to fetus was rarely found during the first eight months of pregnancy, but congenital infection has been demonstrated in about half of the infants exposed during the last two to three weeks of pregnancy. The attack rate after delivery is approximately two-thirds despite prophylactic administration of zoster immune globulin (ZIG) to the infants. The severity of attacks in ZIG protected infants is similar to that in infants protected naturally by maternal antibody. So far about 10 per cent of infants who developed chickenpox in the perinatal period have had attacks of zoster in the first two years of life.

PRODUCTION OF THERAPEUTIC SUBSTANCES

Human growth hormone A total of 29 931 human pituitary glands removed *post mortem* were received by the Therapeutic Products Laboratory at CAMR for processing by two different methods according to whether the glands were frozen or had been treated with acetone. Efforts are being made to encourage hospitals to supply the glands frozen, for higher yields of hormone can be obtained from such material. A total of 311 000 units of this hormone, which is used in the treatment of pituitary dwarfism, were produced during the year.

Asparaginase This enzyme, which is used in the treatment of some forms of leukaemia in children, was extracted and purified by the Therapeutic

Products Laboratory from bulk (400 litre) cultures of a species of *Erwinia* (a bacterial pathogen of plants), prepared by the Microbial Technology Laboratory. CAMR is now the sole source of supply of this enzyme as the only commercial manufacturer (from a different bacterial species) has ceased production. UK hospitals were supplied with 122 megaunits, hospitals in the USA with 152 megaunits and hospitals elsewhere with 85 megaunits.

PRODUCTION OF VACCINES

Tick-borne encephalitis vaccine With the completion of the Immuno building at CAMR, production of tick-borne encephalitis (TBE) vaccine for Immuno Ltd recommenced in Janury 1982 after a two year break. The virus concentrate is prepared by the Vaccine Research and Production Laboratory at CAMR and, after safety testing, is despatched to Austria where it is further processed and ampouled for distribution. It is used to protect those who may be exposed to ticks in the forested areas of Central Europe and 240 litres of the Porton product were accepted for sale in Austria for these purposes.

Anthrax vaccine Although the last batch of anthrax vaccine made in the former Vaccine Unit at Allington Farm (which has since reverted to the Ministry of Defence) is sufficient to last well into 1983, a further batch has been produced in the new Immuno building. The vaccine is used to protect workers at occupational risk of this disease.

PRODUCTION OF OTHER BIOLOGICALS

Tissue cells Virology laboratories (44 PHLS, 31 others) were supplied weekly with cultures of baboon kidney and human fibroblast cells by the Vaccine Research and Production Laboratory at CAMR for use in the detection of virus infections.

Large scale cultures and extracts These have included 21 cultures of human growth hormone in genetically engineered *Escherichia coli* supplied to Kabi-Vitrum AB, Sweden, grown in the Microbial Technology Laboratory, as well as cultures and enzyme preparations for use "in house" and 143 miscellaneous small products, such as cell pastes, for sale to universities and research institutions.

Microbiological reagents Most of the diagnostic reagents used in PHLS laboratories are prepared by the Division of Microbiological Reagents and Quality Control at the Central Public Health Laboratory (CPHL), Colindale. The total volume of bacterial and viral antigens produced was 112

litres, of which 27 litres went to other laboratories; of 47 litres of diagnostic antisera also produced by the Division, 12 litres went to other laboratories. The non-PHLS laboratories are supplied under long standing "grace and favour" arrangements; these cannot be expected to continue indefinitely in times of financial stringency. Material for nearly 4000 Kveim skin tests for sarcoidosis was also issued.

Issue of authentic cultures The National Collection of Type Cultures, of bacteria of importance in medicine (NCTC), supplied 5171 cultures; 16 per cent were sent abroad. This is a further substantial decrease on the 1981/2 figures and probably reflects the effect of the increase in prices made in August 1981. The NCTC is now recognized as an International Depository Authority under the Budapest Treaty and so is entitled to receive patented strains of bacteria for deposit.

SAFETY ASSESSMENT OF LABORATORY EQUIPMENT

Some 33 reports have been issued to the DHSS or manufacturers on the testing by the Environmental Microbiology and Safety Reference Laboratory, CAMR, of the microbiological safety of equipment used in diagnostic laboratories. These have concerned two main types of equipment: sealed centrifuge buckets and rotors, of which one in four models tested proved defective, and equipment used to wash assay plates. Although the latter equipment had the potential to produce aerosols, it was shown in practice to be safe.

EXTERNAL QUALITY ASSESSMENT OF MICROBIOLOGY LABORATORIES

Thirty-four distributions of 115 specimens were made for the National Scheme by the Division of Microbiological Reagents and Quality Control to 457 laboratories in the UK and to 93 laboratories abroad. Nine distributions were made for assessment of virology.

The Research Work of the Service

Some research and development was in progress or completed during the year in nearly all the laboratories of the Service. To report on this work comprehensively would be impracticable within the confines of this Annual Report; the number and main subject headings of the publications by members of the PHLS during 1982 (see Table 2) gives some indication of its size and complexity, which may also be gauged by the amount and variety of the research grants received from bodies which sponsor scientific and medical research (see page 37).

Throughout the existence of the PHLS there has always been sufficient margin in the resources allocated to laboratories to allow some degree of research and development to be conducted alongside their routine service activities as a matter of course. The application of strict cash limits and the reduction in real terms of the funding of the PHLS in recent years, combined with the financial pressures resulting from the increased demand of its service workload (referred to in the previous section of this Report), have so diminished this margin that support for PHLS research projects has to be sought increasingly from external sources, with the delay and uncertainty that this implies. Within these resource constraints, however, many projects large and small have gone ahead; what follows is a highly selective summary of some of them, intended to illustrate rather than catalogue the nature and

Table 2 Publications by PHLS staff in 1982

Subject area	Number of publications
Antimicrobials	36
Cancer research	12
Disinfection	13
Epidemiology	18
Food microbiology	17
Immunology	5
Laboratory safety	7
Specific bacteria and infections	268
Viruses and viral infections	95
Other organisms	44
Techniques	59
Others	17
Total	591

scope of PHLS research and development. The size and complexity of the individual activities concerned varied from small well circumscribed projects performed under supervision by Medical Laboratory Scientific Officers in fulfilment of the requirements of the Special Final Examination of the Institute of Medical Laboratory Sciences, to much larger programmes supported by grants from industry or from various other funding organizations. The smaller projects were particularly numerous in the area and regional laboratories, where they had in common an immediate, practical relevance to improved patient care, by seeking either to increase the precision or efficiency of diagnosis, or an improvement in treatment. Most projects in the former category were designed to develop new, or improve

existing techniques for the serological diagnosis of communicable disease, and in the latter related to the introduction of new antimicrobial drugs, or improved ways of using the older ones. Larger projects were concentrated, as might be expected, in CAMR and CPHL.

EXPERIMENTAL VACCINES

Enterotoxigenic Escherichia coli (ETEC) vaccine Some strains of this common intestinal bacterium produce toxins (enterotoxins) which affect the bowel wall and these ETEC strains are important causes of diarrhoeal disease, especially among the populations of developing countries. Detailed studies in the Division of Enteric Pathogens at Colindale of the factors responsible for adhesion of ETEC to the lining membrane of the intestine, including their genetic control, have led to the development of putative vaccine strains, one of which is being tested in collaboration with the Center for Vaccine Development, Baltimore, USA.

Whooping cough (pertussis) vaccines Vaccines at present used against whooping cough are composed of killed whole bacterial cells of *Bordetella pertussis*. Although current vaccines are reasonably protective and safe, an ambitious programme of research has been in progress in the Pathogenic Microbes Research Laboratory, CAMR, for several years to identify and separate those components of the bacterium that really matter in the production of immunity, with the eventual aim of producing an acellular vaccine (a "cocktail" of the bacterial ingredients essential for protection). Such a vaccine lacking the unnecessary components of the bacterial cell should, in theory, be safer and more effective. This work has advanced to the stage at which discussions are being held with a British pharmaceutical company to assess the feasibility of commercial manufacture of an acellular vaccine based on the techniques developed at CAMR. As a byproduct of this research, a new and more physiological animal infection model is being developed as a possible replacement for the existing standard method of vaccine assay.

Herpes simplex vaccines The commonest manifestation of infection by this virus is "cold sores". The herpes simplex virus type 1 (HSV-1) which causes them is very closely related to another virus, herpes simplex type 2 (HSV-2), which is most often associated with genital herpes, a condition which is not only distressingly recurrent but becoming more prevalent. At the University of Birmingham, Dr G. R. Skinner has prepared an experimental vaccine from HSV-1 treated with acetone to break up the virus particles into subunits. A preliminary trial of this vaccine on a very small scale in sufferers and their "at risk" consorts has reportedly given sufficiently encouraging results to merit further evaluation. In collaboration with Dr Skinner the Vaccine Research and Production Laboratory at CAMR has produced 400 doses of

the vaccine, enough for a clinical trial, and application has been made to the Committee on Safety of Medicines for a Clinical Trial Certificate. Meanwhile research goes on in the Vaccine Research and Production Laboratory to find simpler and higher yielding methods of producing the potentially protective viral subunits.

TRANSMISSABLE DRUG RESISTANCE AMONG BACTERIA

Trimethoprim resistance Monitoring of resistance to antimicrobial drugs among the bacteria causing gastrointestinal infections has been a long standing activity of the Division of Enteric Pathogens at Colindale. Of particular and recent concern has been the marked increase observed in the incidence of trimethoprim resistance in both *Salmonella* and *Shigella* (the dysentery bacilli). Most of this resistance in *Salmonella* occurs in certain types of *S. typhimurium* of bovine origin and reflects the increased use of the drug in animal husbandry. As this drug is also promoted for the treatment of urinary and respiratory tract infections in humans, the emergence of trimethoprim resistance in this familiar way is doubly unfortunate. In the UK, about 60 per cent of the infections with species of *Shigella*, other than *Sh. sonnei*, are acquired abroad, especially in south-eastern Asia; reports from this area also draw attention to increased trimethoprim resistance. The genetic basis of resistance to this antimicrobial is also the subject of study in the Nottingham laboratory.

Methicillin resistance Strains of *Staphylococcus aureus* resistant to penicillin are often susceptible to methicillin, a penicillin antibiotic which withstands the penicillin-destroying enzyme produced by penicillin-resistant staphylococci. Although methicillin resistance among staphylococci has been recognized for many years, its incidence has, with some exceptions, been generally low. Recently, however, it appears to be on the increase, as judged by the antibiotic sensitivity patterns of the strains of *Staph. aureus* sent to the Division of Hospital Infection at Colindale for typing, usually in connection with hospital outbreaks of septic infections. A collaborative study has been set up between the Division, the PHLS Communicable Disease Surveillance Centre (CDSC), the London Hospital and the North East Thames Regional Health Authority to examine the local problem and to collect information on the national prevalence of these strains. These resistant staphylococci are difficult to "fingerprint" with the present set of reagents (bacteriophages); new ones with which to type these staphylococci are being sought so as to allow their spread to be traced more precisely.

Development of a new service For several years hospitals in various parts of the country have been troubled by outbreaks of hospital acquired infection caused by Gram-negative bacteria multiply resistant to antibiotics. This multiple resistance to antimicrobial drugs is genetically determined by the

spread among the bacteria of small portions of extra-chromosomal genetic material (plasmids). Within the Division of Hospital Infection at Colindale a small unit has been formed, the Antibiotic and Chemotherapy Section, which is prepared to assist laboratories investigating outbreaks thought to be associated with plasmid spread, by offering a service to characterize the plasmids which determine antibiotic resistance.

Predictably, antimicrobial resistance among bacteria, and the use of antimicrobials in the prophylaxis and treatment of patients, enjoyed the attention of area and regional laboratories, nine of which reported that they had been engaged in significant research projects related to these topics during the year.

LEGIONNAIRES' DISEASE

Legionellas in water systems The serious bacterial pneumonia known as Legionnaires' disease has proved to be another example of a disease acquired by humans from the inanimate environment and the most important habitats so far identified of the causative bacteria, *L. pneumophila* and related species, are water systems, cooling towers and humidification systems. To discover the extent of the problem and the factors which limit or promote the presence of these organisms in water systems, a collaborative two year survey has been set up, with the assistance of a grant from the DHSS, between the Environmental Microbiology and Safety Reference Laboratory, the CDSC, and the PHLS laboratories at Birmingham, Liverpool and Oxford. Among other PHLS laboratories with a special interest are those at Cambridge, Leeds, Nottingham and Preston. The water systems of hospitals and hotels are under study on a country-wide basis and although the survey is only half completed and the environmental factors have yet to be analysed, the most remarkable finding is the proportion of samples so far found to be positive for *Legionella* (120 of 343). Frequency of environmental contamination of this order and a low background incidence of clinically apparent disease suggest that a particular set of circumstances must obtain to allow infection to occur. Some of the host factors have been identified from previous epidemiological studies; the microbial and environmental factors remain to be elucidated.

Treatment of experimental legionella infections Antibiotic therapy in human legionella infections has given variable and somewhat disappointing results. Clinical experience suggests that erythromycin alone or in combination with rifampicin is best. This combination receives support from work on experimental infections in the Pathogenic Microbes Research Laboratory at CAMR, where rifampicin was shown to be the most effective drug in clearing the organisms from the lungs of animals infected by aerosols of *L. pneumophila*.

DEVELOPMENT OF NEW TECHNICAL METHODS

Detection of bacterial toxins in foods One of the problems in identifying the cause of bacterial food poisoning lies in the slow and complicated procedures necessary for isolating the causative bacteria. Further tests may then be needed to assess their significance. Direct demonstration of the particular bacterial toxin in the suspected food and in patients' faeces would allow the cause of an episode of food poisoning to be identified unequivocally and by using the now well developed technique of enzyme-linked immunosorbent assay (ELISA), the answer may be available in a matter of hours rather than days. Work to this end has been carried out at the Food Hygiene Laboratory, Colindale, in collaboration with the Vaccine Research and Production Laboratory, CAMR, which has undertaken the necessary bulk production of the bacterial enterotoxins. Preliminary results on material from *Clostridium perfringens* food poisoning indicate a high degree of sensitivity for these methods.

Diagnostic kits for hepatitis A and other virus infections Virus laboratories in the Service have long been hampered by the lack of readily available methods for the diagnosis of hepatitis A, the common form of infective jaundice. Work in the Virus Reference Laboratory, Colindale, on the growth of a particular strain of this virus in tissue culture has opened the way for the production of kits using the ELISA principle for the detection of antibodies to hepatitis A virus. Kits prepared by the Division of Microbiological Reagents and Quality Control are undergoing trial and are expected to be in routine use shortly. By this means, in addition to diagnosing individual cases, it should be possible to reduce the amount of immunoglobulin given to travellers to high risk areas by giving it only to those who are not already immune.

Other diagnostic kits developed at Colindale which make use of the ELISA principle and which will be ready for general use in the PHLS in the immediate future include one for the detection of rotavirus, an important cause of gastroenteritis in young children. Rotavirus infections are currently detected by electron microscopy of the faeces; the use of these kits should reduce wear and tear on these expensive instruments and mean that such outbreaks can be investigated more widely.

Other applications of the ELISA principle These are being developed as aids for the early diagnosis of two fungal infections (aspergillosis and candidiasis) at the PHLS Mycological Reference Laboratory and also, through work at the PHLS Leptospira Reference Unit, are expected to replace the present method (complement fixation) for testing for antibodies to the common types of leptospires. These and other serological techniques are an area of special interest and study in the area and regional laboratories, six of which reported that they were engaged in research on this subject during 1982/3.

NEW TECHNOLOGIES

Medical microbiologists are sometimes criticised for being slow to exploit discoveries in molecular biology or other areas of science in the advancement of their subject. Whether this criticism is justified or not, two of the more important, monoclonal antibodies and gene probes, figure in research and development projects in several parts of the PHLS. Monoclonal antibodies have already been developed for use in many areas and their numbers grow rapidly. The problem is one of co-ordination to avoid wasteful duplication. Hitherto those working with these new immunological tools in the Service have exchanged information and ideas in an informal working group. Development and application has now reached the stage at which some concentration and regularization of production has become desirable and the Board is taking steps to this end. The main activity in this field has taken place in CAMR and CPHL, though a few regional and area laboratories have also begun to join in.

The second of these new technologies is being applied in other laboratories of the Service as well as at the Molecular Genetics Laboratory at CAMR, where the use of gene probes is an integral part of the scientific programme. They have contributed to an understanding of the structural proteins of Lassa virus and the detection of toxin and other genes in *Escherichia coli*, to give but two examples.

Under this heading must also be considered the beginnings of the introduction of automation into microbiology. Developments in this field have been slow, perhaps because of the exquisite sensitivity of traditional methods by comparison, until very recently, with standard physical or chemical techniques. An automated method for examining blood cultures using electrical impedence as an index of bacterial multiplication shows some promise, and was under investigation in Cambridge, and the Oxford laboratory has continued its assessment of an alternative automated technique for this type of examination.

DENTAL MICROBIOLOGY

Dental caries Studies have been made of the effect of two inhibitors used in preventive dentistry, fluoride and chlorhexidine, on the metabolism of oral bacteria. Combinations of these two were shown to have an additive inhibitory effect on acid production by oral streptococci. The Pathogenic Microbes Research Laboratory at CAMR is pursuing further studies on the regulatory mechanisms affecting the enyzmes responsible for the breakdown of sugars by oral bacteria and has established defined, mixed communities of nine species of oral bacteria under conditions of continuous culture to observe their interaction. Field studies are under way in this laboratory in collaboration with the Bath Health District, the Eastman Dental Hospital and the Department of Oral Biology, University of Leeds,

to investigate the relationship between the species of bacteria which make up dental plaque and the beginning of the carious process and the level of fluoride in the water supply to that in the tooth enamel.

Periodontal disease The technique of continuous culture under chemically defined conditions has been applied for the first time to a fastidious species of bacterium which grows only in the absence of oxygen and which is implicated in disease of the gums. These studies are aimed at elucidating the factors which determine its capacity to cause disease; one of these has been provisionally identified so far.

CANCER

Possible roles for bacteria Many years work in the Bacterial Metabolism Research Laboratory, supported by the Cancer Research Campaign, has led to the hypothesis that cancer of the large bowel may result from the chemical byproducts of bacterial attack on the bile acids by certain anaerobic bacteria (referred to as NCD) and that the combination of high bile acid concentration in the bowel and the carriage of NCD indicates an increased risk of developing cancer of the large bowel. The value of these two factors as a pointer to the likelihood of cancer developing is being studied prospectively in a long term follow up of a "normal" population in comparison to various "at risk" groups. This laboratory is also investigating the role of bacteria in gastric juice in the formation of *N*-nitroso compounds from dietary nitrate as a possible causative factor in cancer of the stomach, and a pilot study has begun to test the hypothesis that some female sex hormones formed in the bowel by bacterial action on intestinal steroids might promote some varieties of tumour of the breast.

Possible roles for viruses Apart from a long term follow up of students who have experienced infection with Epstein-Barr virus, which causes infectious mononucleosis ("glandular fever") in adolescents and adults and is associated with Burkitt's lymphoma (a tumour of the jaw) in Central Africa, most of the studies have been made at the level of molecular genetics. Work in the Molecular Genetics Laboratory at CAMR has concentrated on human cytomegalovirus (HCMV), a virus of the herpesvirus group and on a group of viruses, the polyomaviruses, several of the human strains of which were first identified by the Virus Reference Laboratory, Colindale. Structural analysis has been made of the portion of the genetic material of the virus which is responsible for transforming cells in tissue culture into the "malignant" state and a search is being made for HCMV nucleic acids in samples of tumours from a rare form of cancer in Africans (Kaposi's sarcoma). Tumours of this kind are encountered in the recently described acquired immune deficiency syndrome (AIDS). Although polyomaviruses are not, as far as is known, associated with malignant disease in humans, there is such

an association in animals. Close genetic analysis has already revealed differences between human strains originally isolated from widely different disorders.

ENZYME RESEARCH

Fibrinolytic enzymes Apparently unique and previously unknown activators of plasminogen (one of the many factors concerned in the mechanism of blood clotting) have been extracted from two sorts of tissue culture cell lines, one of human breast epithelium, the other of guinea-pig skin. These may prove to be valuable as diagnostic and therapeutic aids in the management of thrombotic disorders and much effort is currently being devoted in the Microbial Technology Laboratory at CAMR to scaling up their production and purifying them.

Carboxypeptidase Patients treated with methotrexate, an anti-cancer drug, often suffer severely from its toxic side effects and trial of this enzyme prepared from a species of *Pseudomonas* showed that methotrexate in the blood was broken down by it. The gene concerned in the pseudomonad was successfully inserted into a strain of *Escherichia coli* and this has allowed what appears to be the same enzyme to be produced on a much larger scale. Once this material has passed its toxicity tests, it will be introduced for clinical assessment. This particular carboxypeptidase (CPG_2) has also been shown in a collaborative study with Charing Cross Hospital, London to inhibit the growth, in the laboratory, of cells from a rare form of human cancer (chorioncarcinoma).

Phenylalanine ammonia lyase (PAL) The amino acid phenylalanine is a normal dietary constituent but sufferers from phenylketonuria, an inborn metabolic disorder, must avoid it. The addition of PAL to the food of these patients should, in theory, break down the phenyalanine and thus obviate the need for dietary restriction. However, PAL is itself broken down by digestive secretions and the Therapeutic Products Laboratory at CAMR has been carrying out work on preparations of this enzyme in strains of yeasts, some of which are more resistant to digestive attack. Resort has been had to genetic engineering in an attempt to boost the yield of PAL from such strains.

MICROBIAL DEGRADATION OF PERSISTENT TOXIC ORGANIC MATERIALS AND METALS

The Microbial Technology Laboratory at CAMR, supported by the Department of the Environment, has been engaged on work to discover ways in which certain chemical contaminants of the environment might be detoxified by microbial action. Limited progress on this ambitious project has

been made on the following substances: dieldrin, cadmium, chlorobenzoic acids and polychlorinated biphenyls.

MOLECULAR GENETICS

Increasingly this area of molecular biology is contributing to the advancement of medical microbiology through its ability to shed light on fundamental problems associated with pathogenicity. At CAMR in the Molecular Genetics Laboratory the substantial research effort being made to understand the structure and function of the genetic components of human cytomegalovirus has already been referred to. Infection by this virus takes many forms, from the symptomless to the most severe. In particular its role in causing congenital infections, often associated with mental retardation, and in infections in patients where immunological mechanisms have been depressed, is poorly understood. The possibility of being able to distinguish between different human strains is opened up by the studies being made on this virus at the molecular level.

The ability to insert genetic information concerning a human virus into a bacterial cell and thereby cause the bacteria to produce the viral product specified by that genetic material is now commonplace. A striking illustration of its reality is to be seen in the electron photomicrographs (Figure 2) made in the Virus Reference Laboratory at Colindale, which show side by side the core antigen of hepatitis B virus as found in the serum of a patient and the same antigen as produced by the "genetically engineered" intestinal bacterium, *Escherichia coli*.

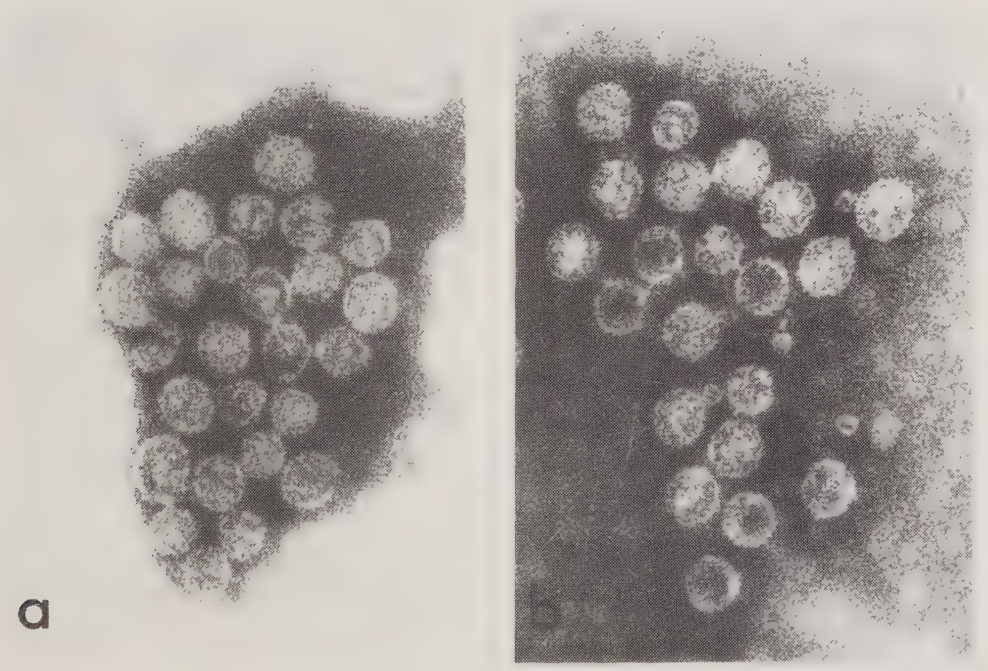

Figure 2 Preparations of (a) *Escherichia coli*- and (b) human liver-derived HBc antigen aggregated by human anti-HBc IgG. ×189 000. [Reproduced by permission of Macmillan Journals Ltd from B. J. Cohen and J. E. Richmond (1982) *Nature, Lond.*, **296**, 677–678.]

A NEWLY EMERGENT DISEASE

Considerable interest has been aroused in "toxic shock syndrome" (TSS), first named in the USA in 1978, which affected women who used intravaginal tampons, especially of one particular brand (not sold in the UK), following the discovery that the illness was an unusual, and sometimes fatal, manifestation of staphylococcal infection. With the help of a research grant from Proctor and Gamble, work has proceeded at Colindale in the Division of Hospital Infection in collaboration with the Food Hygiene Laboratory on the toxin produced by the strains of *Staphylococcus aureus* isolated from sufferers from this condition. It appears indistinguishable from the staphylococcal enterotoxin F associated with staphylococcal food poisoning. The role of this toxin in TSS and in staphylococcal pneumonia is under investigation; meanwhile a test for antibody to it has been developed and this has shown that antibody is absent in patients as compared with normal persons. At the time of this Report, 53 confirmed cases have been identified.

A VIRUS IN SEARCH OF A DISEASE

Human serum parvovirus (HSPV), a small round virus, was discovered in 1975 by Dr Y. E. Cossart of the Virus Reference Laboratory at Colindale while working on hepatitis. It was not linked with disease until recently, when it was shown to be associated with episodes of bone marrow failure (aplastic crises) in patients affected with the hereditary "sickle cell" trait in their red blood cells. Work to develop diagnostic assays for this virus has led to its recognition as the cause of a mild feverish illness with rash (likened to a "slapped cheek") in children, known as erythema infectiosum or "fifth disease", which occurs in epidemics. Biochemical analyses of HSPV have clarified its classification as a parvovirus and the use of monoclonal antibodies and radioisotopes has allowed rapid progress to be made on investigation of this virus, which is particularly difficult to handle as it has not yet been cultivated in the laboratory. Source material is therefore strictly limited.

A NEW GENITAL PATHOGEN?

The identification of *Gardnerella vaginalis* as a possible pathogen of the female genital tract has attracted the interest of many area and regional laboratories, some of which have set up and are continuing studies of the distribution of the organism in different populations of women with and without vaginal symptoms.

This development illustrates how the diagnostic work of the Service becomes more complex and technically demanding year by year. Clinical and environmental specimens are now examined for many times the number of specific pathogens than were thought to exist twenty years ago, and if

anything the process is still accelerating. The implications of these developments for the revenue and capital costs of any clinical microbiological service, and of the PHLS with its particular epidemiological commitment, are obvious.

Administrative and Financial Aspects of the Service

FINANCE

The DHSS's net cash allocation to the Board for 1982/3 was £24.7 million (excluding finance for special capital schemes). This was augmented by a further £5.8 million from the Board's own income generating activities, permitting a total gross expenditure funding of some £30.5 million.

It is interesting to compare these figures with the two previous financial years, during which time the PHLS ceased to be volume funded and the system of cash limits was imposed. In the year to 31 March 1982 the comparable net cash allocation was £23.7 million and to 31 March 1981 it amounted to £21.9 million. Thus the rate of Government funding slowed from an 8.2 per cent increase in 1981/2 to 4.2 per cent in 1982/3. However, in 1982/3 costs associated with both pay and non-pay items increased on average by 7 per cent, which resulted in severe financial problems in the Service. By restricting the filling of staff vacancies, encouraging early retirement and improving financial control over the Board's operations, the overspend was held to £3000 on gross expenditure.

Figure 3 illustrates where the revenue funds received by the PHLS were spent. Pay accounted for approximately 70 per cent of the total expenditure. Laboratory consumable supplies was the next highest item at 12 per cent,

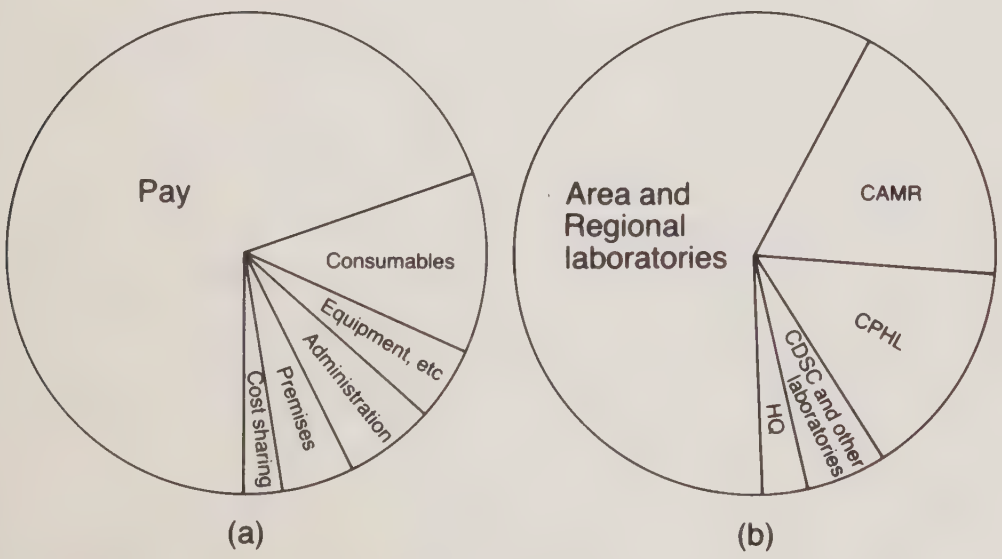

Figure 3 Where revenue funds were spent: (a) expenditure by item; (b) expenditure by unit.

followed by administrative costs, such as those relating to travel, meetings, postage and telephones, at 6 per cent. Turning to expenditure by unit, the area and regional laboratories accounted for almost 60 per cent of the funds. The central services provided by the Central Public Health Laboratory, the PHLS Centre for Applied Microbiology and Research and the PHLS Communicable Disease Surveillance Centre amounted to slightly more than 36 per cent, with Headquarters costs, including Computer Services, at approximately 4 per cent.

To summarize, the PHLS began to experience the effects of reduced cash limits in the year under review. Tight financial control over all aspects, but particularly that of staffing, enabled the Board to keep within this reduced level of funding.

INCOME GENERATION

Income accruing to the Board amounted to £5.8 million in the year under review. Comparable figures for the year to 31 March 1982 were £5.1 million and to 31 March 1981 £3.8 million, giving year on year increases of 14 and 34 per cent respectively.

Income from the sale of products, cultures and reagents, mainly generated by the laboratories at CAMR, totalled £1.14 million for the year to 31 March 1983 for the whole of the PHLS, compared with £982 000 in 1981/2, an increase of 16 per cent. The other main income producing activities, totalling £4.6 million, included royalties, fees, the sale of Central Supply Services to other bodies, grants from other organizations and rechargeable salaries and services to the NHS in connection with joint laboratories. Further details are contained in the Annual Accounts on pages 67–69.

As mentioned in the Statement of the Chairman of the Board, the Parliamentary Under Secretary of State for Health, Lord Trefgarne, visited Colindale, the PHLS laboratory at Guildford and CAMR. An important outcome of the visit to CAMR was that permission was given by the Department for the Board to retain, through the Appropriation in Aid procedure, some of its income for the purpose of generating future income.

The Steering Committee on Income Generating Activities (SCIGA) continued under the Chairmanship of Professor Richmond, FRS. The way was cleared for a submission to the Department of Industry (DOI) for a Fermentation Technology Development Project costing £2 million. SCIGA also approved a proposal to set up a National Cell Depository at CAMR, with long term funding from the DOI. The DOI accepted these proposals and work has since started on the two projects at Porton.

Future potential income from royalties was enhanced by several agreements signed during the year. An example was that with Cambridge Life Sciences concerning "A method for the estimation of *N*-acylated primary aromatic amines" (see pages 50–52).

Finally the Board approved a report from Coopers and Lybrand on the costing of projects. Reliable costing together with the production of trading accounts commenced at CAMR on 1 April 1983.

GRANTS FROM OTHER ORGANIZATIONS

The Annual Accounts on pages 67–69 show the sums received by the Board in the form of grants. Grants are used to employ staff on short term contracts and to pay for equipment and laboratory consumables on specific areas of work. The main bodies from which grants were received and the amounts given are shown in Table 3. In 1981/2 the total of grants received amounted to £497 998.

Table 3 Grants received by the PHLS during 1982/3

Grant-giving body	Funds received (£)
World Health Organization	25 162
Medical Research Council	176 550
Cancer Research Campaign	188 504
Other bodies	262 440
Total	£652 656

CAPITAL PROJECTS

Major capital schemes The highlight of the year was the laying of the stone commemorating the start of the New Colindale by the previous Director of the Service, Sir Robert Williams, on 28 October 1982. The Chairman made a presentation to Lady Williams at the reception afterwards. As reported last year, work commenced on the project in March 1981 and the building was "topped out" by the Director of the Service, Dr Whitehead, in August 1982. The contract continues on schedule for completion in November 1984.

The Board received Departmental approval to build a Production Centre at CAMR towards the end of the year at a contract price of £3.1 million. It is hoped to complete the project by the end of 1984. Design work continued on a new Fermentation Pilot Plant, and approval, in principle, was given by the Department. In order to allow these two major schemes to go ahead design work on new primary services at CAMR to update the boiler house, electricity and sewerage commenced.

Regular capital building projects and laboratory developments During the year, a number of changes both geographical and physical were made to the laboratories. In April 1982 work started on the new joint laboratory at the new William Harvey Hospital, Ashford, Kent. It is expected that it will be completed in about 20 months, when the PHLS laboratory at Maidstone will move to Ashford. The PHLS Leptospira Reference Laboratory moved from Colindale to the PHLS laboratory at Hereford. The new accommodation for the laboratory was provided at a net cost to the Board of £120 000 and was opened in May 1982. On 14 April 1983 the Chairman opened a new building for the PHLS laboratory at Gloucester, costing £420 000.

In addition the following laboratory building projects were completed during the year. The net costs of the schemes are shown in parenthesis. Alterations were carried out to the bacteriology section at Epsom (£145 000) and the special pathogens laboratories in Leeds (£135 000), Birmingham (£100 000) and Liverpool (£80 000). Work was finished on extensions to the laboratories at Cambridge (£75 000), Peterborough (£80 000) and Norwich (£50 000) and upgrading was completed at Preston (£22 000). At CAMR, work was finished on the Bacterial Metabolism Research Laboratory, which was moved from Colindale in February 1982, and on the Therapeutic Products Laboratory, at a combined cost of £140 000.

The Board decided to devolve its reference facilities for treponemal serology from the PHLS Venereal Diseases Reference Laboratory at Whitechapel to seven laboratories and to transfer the gonococcus reference service to a new PHLS Gonococcus Reference Unit established in the PHLS laboratory at Bristol. A year's notice was given of these arrangements which came into effect on 1 October 1983.

LABORATORY EQUIPMENT

An Equipment Evaluation Group was formed at the beginning of 1982 to explore ways of providing advice to laboratory directors about obtaining value for money on equipment purchases. The need for such advice arises for several reasons, among which are that laboratory equipment already accounts for significant annual expenditure at a time of diminishing financial resources and there is also an increasing demand from laboratories for the introduction of new technology.

During the initial meetings, the Group rejected lengthy evaluation procedures in favour of a relatively simple consumer-survey approach because equipment is changing rapidly and there is no benefit in advising Directors about equipment that has been superseded by newer models. Information about equipment was gathered by questionnaire with the emphasis on such practicalities as operating costs, reliability and ease of operation.

The results of the first survey were published in a newsletter during the year and covered carbon dioxide incubators, multi-channel pipetters,

bench-top centrifuges and deep freezes. Work has started on the preparation of the second newsletter which is to be devoted to ELISA readers and washers. In addition to this kind of information, the newsletter is used for general comment about trials and safety aspects of equipment.

COMPUTER SERVICES

The demands of the Computer Services continued to increase through the year. In March and April 1982 a dual processor CTL 8066 was acquired for the New Colindale laboratory and installed in advance at Headquarters. The new computer eased the load on the existing equipment and encouraged the development of scientific and administrative systems.

The National External Quality Assessment Scheme was developed for the Division of Microbiological Reagents and Quality Control to run on the equipment at the Central Public Health Laboratory, Colindale, and laboratory staff now input their information directly, thus reducing the need for data preparation. An assessment of the needs of virology quality assessment was also made. Other scientific systems continued to run successfully, and the use of wordprocessing is firmly established.

The CTL Modular 1 is too small to accommodate further work at CAMR although existing systems continue to operate successfully. Most laboratories have turned to microcomputers to meet their requirements and Computer Services installed systems for the Bacterial Metabolism Research Laboratory and the Pathogenic Microbes Research Laboratory using data-base and wordprocessing packages.

Many area and regional laboratories received help with microcomputer data handling systems. During the year greater use was made of commercial data-base software to speed development times and allow laboratories more flexibility. The development of Microlab – a system for PHLS use – at the Norwich and Leicester laboratories continued and the complexity of requirements indicated further work.

On the administrative side, Computer Services provided programs for the analysis of the new workload statistics information. A management information system was developed at Headquarters to maintain details of staffing levels within the Service.

During the year a terminal for on-line literature searching was installed in the Central Library at Colindale. The library now has access to the files of *Index Medicus*, *Exerpta Medica* and many other data-bases. A reader–printer for microfilm and microfiche has also been acquired to cope with the growing amount of literature available in this form.

STAFF MATTERS

Because of the financial strictures imposed at the beginning of the year a scheme for voluntary premature retirement was issued by the NHSS Super-

annuation Branch. This was widely publicised throughout the Service and 19 staff availed themselves of the terms. In addition the filling of vacancies was severely restricted throughout the Service. As shown in Table 4, these policies resulted in a reduction in overall staff numbers of 3 per cent through natural wastage.

During the year a staff management information system was developed. It is now an integral part of the Personnel Department at Headquarters and is a

Table 4 Numbers and grades of staff employed by the PHLS as at 31 March 1983 (in whole-time equivalents) [a]

	Staff numbers at 31 March 1983						Total staff numbers as at 31 March 1982
	Regional and area laboratories	CPHL	CAMR	CDSC	HQ	Total	
Consultants	88	13	3	5	3	112	112
Other medical	41	6	2	2	-	51	60
Top Grade and Principal Microbiologists	14	17	28	-	1	60	62
Other microbiologists	41	43	65	1	-	150	150
Technical Officers, Principal and Senior Chief MLSOs	53	8	2	-	-	63	70
Other MLSOs and works staff	757	60	64	1	-	882	869
Administrative and clerical	223	67	31	21	61	403	371
Ancillary staff and others	204	85	110	-	8	407	500
Totals	1421	299	305	30	73	2128	2194

[a] In addition there were 744 staff working in PHLS laboratories employed by the Regional or District Health Authorities. This includes 61 Honorary appointments. The figures exclude staff on short term contracts and employed on specially funded projects.

vital tool in the control of staffing levels. The system has allowed establishment data to be computerized, thus replacing previous manual methods. It is hoped to continue to develop the system in conjunction with the payroll section.

Policies covering discipline and grievance procedures were approved by the Board after full consultation with the recognized Whitley trade unions and staff associations. They apply to all staff in the Service.

As reported previously, the PHLS formally applied for admission to the NHS Whitley Council in March 1981. Although Board representation was secured on the PTB Council, admission to PTA was not obtained until the summer of 1983.

Negotiations began during the year between the DHSS and the appropriate Whitley staff side representatives for the undertaking of a major departmental review of the PHLS. The Service is classified as a centrally funded non-departmental public body, although the terms and conditions of staff are identical to those of the NHS and the Board follows Whitley agreements. The aims of the review were "to review the effective, efficient and economic operation of the PHLS, including its functions and their most appropriate organisation and staffing in terms of numbers, grades and manpower costs". The review began in April 1983 and it is expected to be completed in about one year.

VISITS TO THE THIRD WORLD

Visits to the Third World countries were made by a number of staff. Some instances are given below:

Dr B. Rowe, funded by WHO, visited Santiago, Chile, as a WHO/PAHO Consultant to establish an *Escherichia coli* Laboratory in the Institute of Public Health.

Dr Marguerite Pereira, funded by WHO, attended an Influenza Workshop comprising WHO/China talks and a meeting on the origin of pandemic influenza, Beijing. Dr Periera also made a visit to pioneer areas near Beijing to see an expanded programme of immunization.

Dr C. L. R. Bartlett made a survey of cooling water systems in the Middle East and trials of biocides in Abu Dhabi, Dubai and Bahrain, funded by the commercial company Houseman (Burnham) Limited.

Mr J. F. H. Peel, funded by WHO, visited Cairo, Egypt, for technical discussions and design study on a containment laboratory and advising on constructing and equipment a Class III laboratory. Mr Peel also made a visit to Lagos, Nigeria, for technical discussions on constructing and equipping of a high security laboratory; this second visit was funded by Comprehensive Services International Lagos.

Dr R. T. Mayon-White visited South Yemen to assist in the investigation of diphtheria at the expense of WHO.

Miss Betty Whyte

The PHLS Central Library at Colindale has achieved a high standing among scientific libraries, in the specialist field of medical microbiology. This pre-eminence is, in the main, attributable to the skilled professionalism and remarkable insight of Miss Betty Whyte, its former Librarian. Under her guidance, the Library has become a precious research tool and, in consequence, a national resource. Betty was appointed Librarian in July 1948 and supervised its continual growth until her retirement in August 1982. In Figure 4 she is shown receiving a gift marking the gratitude of present and former members of the Service, from Sir Graham Wilson, FRS, who was Director of the Service from 1941 to 1963.

Figure 4 Miss Betty Whyte and Sir Graham Wilson, FRS.

Special Topics

STREPTOCOCCI CAUSING INFECTIONS IN INSTITUTIONS

Dr G. Colman and Dr E. Mary Cooke

Division of Hospital Infection, Central Public Health Laboratory, Colindale Avenue, London NW9 5HT

The major human pathogen among the streptococci remains that of Lancefield group A – the group A streptococcus. This organism is widely distributed in the community and during winter as many as one child in 20 may carry it. The most common infections are sore throat and septic infection of the skin (pyoderma). Sore throats are common in young people and because infection is spread by secretions from nose and throat, outbreaks occur sporadically in residential institutions. Thus epidemics are to be expected (and do occur) in boarding schools, in detention centres for young offenders and in military training establishments.

Streptococci also of group A, but usually of other types than those which cause sore throats, can infect damaged skin, causing pyoderma. Outbreaks of skin sepsis occur in places where people with damaged skin work or play together. These include rugby clubs, abattoirs and institutions in which physical training in an important activity.

Uncomplicated streptococcal infections respond to antibiotic treatment and rarely need hospital care. Rheumatic fever and acute glomerulonephritis which may follow streptococcal infections are, however, serious; fortunately in this country they are uncommon complications of otherwise simple infections. Streptococci of particular types tend to be more associated with these serious complcations. Strains of a type particularly associated with glomerulonephritis are currently widely distributed in England and Wales. Cases of acute glomerulonephritis are occurring in, for example, detention centres. On the other hand, in a large outbreak of pyoderma which occurred in 1979 and 1980 in a military training establishment where there were some 1300 known infections, no case of glomerulonephritis or rheumatic fever occurred. Studies revealed that two infecting strains causing this outbreak were representative of new types which appear to lack the ability to cause these complications.

In attempting to elucidate the epidemiology and pathogenicity of streptococci, the typing systems developed and maintained by the PHLS provide essential laboratory backing for investigations aimed at the control and

prevention of these infections which may sometimes have serious consequences for those in institutional care.

FREE-LIVING AMOEBAE IN BATH – THE OUTCOME OF A CASE OF MENINGITIS

Dr P. G. Mann
Public Health Laboratory, Royal United Hospital, Bath BA1 3NG

and Dr D. C. Warhurst
Amoebiasis Unit and PHLS Malaria Reference Laboratory, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT

"All our lives are a going out to a place of execution, to death"

John Donne

In 1978 a child died in Bath from primary amoebic meningitis (PAM). A family tragedy, this event had several important consequences, including some outside medical protozoology. The child was admitted to hospital with a short history suggesting meningitis. Examination of the cerebrospinal fluid (CSF) confirmed the diagnosis as pyogenic meningitis but did not disclose a causative organism. Despite broad-spectrum antibacterial chemotherapy the illness progressed and a second sample of CSF was submitted. This time an alert Medical Laboratory Scientific Officer drew attention to unusual motile cells seen during a routine cell count. But for this the case would have gone undiagnosed, as have several reported cases whose nature has only been established by re-examination of autopsy material years after death.

Once amoebic meningitis was suspected, advice on treatment was quickly provided from the PHLS laboratory, Bristol (where similar cases occurred in 1969), from the PHLS Communicable Disease Surveillance Centre and from the Amoebiasis Unit of the Hospital for Tropical Diseases, London. Treatment was unavailing, but investigation led to identification of *Naegleria fowleri* in two specimens of CSF, as well as the demonstration of characteristic findings in post-mortem brain tissue.

Although PAM has been reported worldwide, it is less rare than the number of reported cases suggests and in several countries clusters of cases have arisen from a common source; such episodes have been controlled by protective measures which recognize that infection is acquired by inhaling warm, polluted water, usually while bathing. Whenever a case is diagnosed efforts must be made to identify the source of infection so that immediate preventive action can be taken. In Bath the likely source was a public swimming-pool supplied with warm water from hot springs, which also supplied several recreational pools and a hydrotherapy pool. Examination of the thermal spring complex revealed free-living amoebae, identified as environmental strains of *N. fowleri*. On advice, the authorities cut off the

Figure 5 A late 17th Century scene at the King's Bath.

supply of spring water. One recreational pool and the hydrotherapy pool were provided instead with mains water. Three other pools were closed. Visitors to the Roman Baths were warned against dabbling their hands in the water.

There were further consequences. The search for amoebae necessitated draining the mediaeval King's Bath (Figure 5) to get to the Roman spring beneath and the foundations of the 18th Century Pump Room thus revealed were seen to be seriously eroded. Extensive underpinning was needed which required removal of the floor of the King's Bath, thereby exposing the site of the Roman spring. This in turn permitted archaeologists to explore a temple complex long known to be lying beneath the Pump Room. Safety measures were devised to protect the engineers and archaeologists working in potentially infective warm mud or water.

Meanwhile international studies of environmental strains of *Naegleria* had led to the recognition of a new species, *N. lovaniensis*. This is closely related to *N. fowleri* and found in similar situations, but is non-pathogenic. Re-examination of the Bath 1978 environmental isolates showed them to be *N. lovaniensis*. Regular sampling of the hot springs began in June 1981, material from five sites being examined fortnightly. *N. lovaniensis* was recovered regularly, until December 1981, when isolations of *N. fowleri* were first made. The sampling continued until April 1983 with no further positive

findings. Efforts were then concentrated on two sites where temperatures fluctuated under the influence of the weather and in June 1983 three strains of *N. fowleri* were recovered from one site, so confirming the presence of pathogenic amoebae in the spring system and justifying the preventive measures.

Closure of the baths led to a demand for their restitution, with a new supply of unpolluted spa water. The original springs rise from a deep aquifer, up a fault under the Pump Room, acquiring their amoebae as the water issues from a bed of river gravels. After several trial bores it was finally possible to drill obliquely at one side of the fault, reaching the thermal aquifer at a depth of 80 metres under a layer of rhaetic clay (Figure 6). As a result hot spa water is now available uncontaminated by the amoebae resident in the gravels where the Roman springs rise. The bore was sunk with stringent precautions against carrying infection from the surface into the aquifer.

Investigating this fatal case did more than reveal amoebae in the springs and show why the disease was rare although the pathogen was widespread. Searching for the source of the amoebae revealed erosion of the Pump Room foundations. Essential repairs facilitated the exposure of a buried Roman temple. Unavoidable preventive precautions catalysed a major reconstruction project. The sinking of a new borehole to supply unpolluted spa water enhanced knowledge of the fault structure and aquifers beneath the city of Bath.

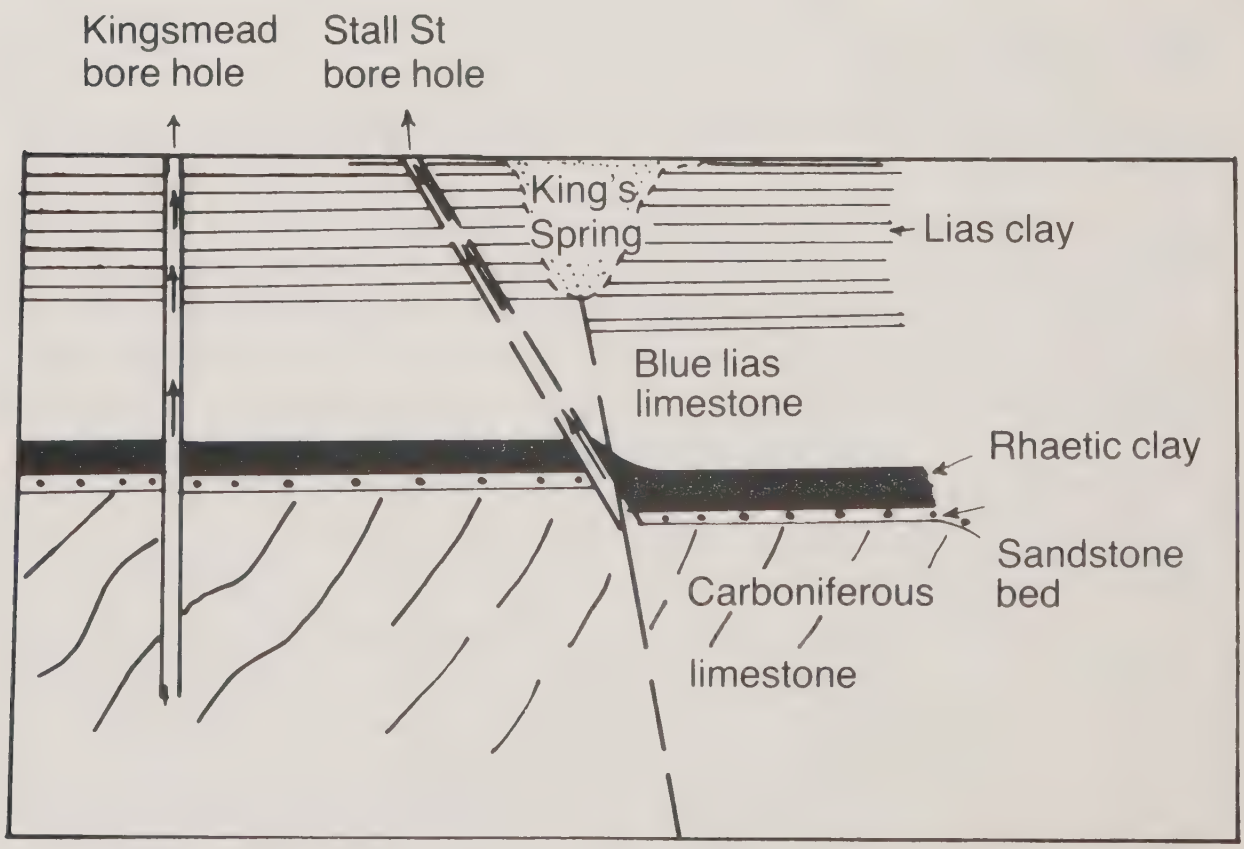

Figure 6 The new borehole sunk to bypass the infected springs at Bath spa, showing also one of the trial bores (Kingsmead bore).

One final outcome was characteristic of the PHLS. An informal working group on free-living amoebae was formed to promote awareness of these organisms, and of the simple skills needed for their recognition and isolation, in the hope that in future fewer cases will be missed and that early diagnosis may yet save a life.

This investigation has been a team effort, but special acknowledgment must be made to Mr A. Yates who first saw the amoebae, to Mr V. Oreffo who first grew them from CSF and to Mr S. Kilvington who made the first environmental isolates.

TOXOPLASMAS AND TRANSPLANTATION

Dr D. G. Fleck

Public Health Laboratory, St George's Hospital, London SW17 0QT

The first case of disseminated toxoplasma infection following cardiac transplantation in the UK was observed by Dr P. G. I. Stovin in Papworth Hospital, Cambridge in October 1981. Following observation and isolation of toxoplasma organisms from the biopsy and post-mortem material from this patient, the PHLS laboratories at Cambridge and Tooting mounted a study of cardiac transplant patients similar to one carried out in the USA. The American work has shown that disseminated toxoplasmosis appears when heart muscle from an antibody-positive donor is given to an antibody-negative recipient. About 10 per cent of deaths due to infection following cardiac transplant are caused by toxoplasmas.

Of 41 patients receiving heart transplants at Papworth, about 16 (40 per cent) had antibody to toxoplasma and this was taken to indicate pre-existing immunity to infection with toxoplasma. Among donors, about the same percentage had toxoplasma antibody. In four instances a heart from an antibody-positive donor was transplanted into an antibody-negative recipient. Two of the recipients developed toxoplasmosis (although in the second case this was not demonstrated by isolation of the organism), the third died eight days postoperatively from acute rejection and the fourth is alive and well.

It is not practicable to exclude donors with toxoplasma antibody because of the shortage of donor material, but foreknowledge of the event may allow drugs to be used to control the infection. More needs to be known about the prevalence of toxoplasma organisms in transplantable tissue (especially cardiac muscle) and about diagnosis and treatment of this infection.

The organism (*Toxoplasma gondii*) is a parasite unable to grow outside nucleated cells. It is spread from host to host by carnivorism, such as cats feeding on birds and mice, and by cystic forms of the parasite which develop in the feline gut. The cat is the most important host because a sexual cycle occurs in the cells of the intestine of the cat with the production of a cyst more resistant to the environment than the other forms of the parasite. The

cyst is passed by the cat in its faeces and can survive for a year or more in soil and may infect other animals. Man may become infected via uncooked vegetables and unwashed hands. The degree of risk of these various modes of spread has yet to be quantified.

The damage done to human patients by the parasite is usually small. If, however, the organism infects a pregnant woman there is a risk (higher in the first three months of pregnancy) of infection of the fetus via the placenta, producing, in a few cases, hydrocephalus, blindness and mental subnormality. In other cases retinitis may lead to visual disturbance in later childhood. The extent of this disability in the population needs further assessment.

Toxoplasma infection is widespread throughout the world, especially in warm, wet climates, so that control of the spread of the infection is difficult. The persistence of the organism in human tissues becomes a threat when the immune mechanism of the host is altered by drugs (as in organ transplantation) or by other conditions. Acquired immune deficiency syndrome (AIDS) is probably caused by an infectious agent which has a profound effect on the immune mechanisms of the patient. Immune suppression allows normally quiescent organisms such as cytomegalovirus and pneumocystis, as well as toxoplasma, to disseminate into unusual sites for these organisms, thereby producing aberrant clinical manifestations. In the case of toxoplasmosis, neurological complications such as brain abscesses may occur. Toxoplasma infection may itself cause some, usually mild, immunosuppression. Occasionally this may lead to disseminated infection which is difficult to diagnose and treat.

It is likely that the host defence to this complicated infective process is more dependent on the cellular immune mechanisms (macrophages, T-cells) than on antibody circulating in the blood. More work is needed in this direction and on the development of more effective drugs, or of vaccines with which to combat this insidious parasite.

INFLUENZA RESEARCH AT GUILDFORD – A LONG TERM STUDY

Dr Joan R Davies

PHLS Influenza Research Unit, Public Health Laboratory, St Luke's Hospital, Guildford GU1 3NT

The Religious, Royal and Ancient Foundation of Christ's Hospital is a boarding school for some 800 boys, in rural Sussex. In 1970 a controlled trial of inactivated influenza vaccines was set up by the Epidemiological Research Laboratory with the collaboration of the school medical officer, Dr T. W. Hoskins, and the PHLS laboratory at Guildford. The first results were encouraging; boys who had been vaccinated had lower attack rates during outbreaks of influenza A and influenza B than those who had not

received appropriate vaccine. The vaccine trial was terminated and all boys were offered annual vaccination against influenza. However, the study of the epidemiology of influenza in the school was continued.

It soon became apparent that outbreaks of influenza were still occurring even though over 90 per cent of the boys had been vaccinated. The reasons for this disappointing result were studied by the PHLS Influenza Research Unit, established in the Guildford laboratory in 1978.

It was shown that natural infection induced satisfactory immunity, usually sufficient to protect a boy from suffering a further attack of influenza of the same sub-type throughout his school career. The immunity conferred by the vaccine was short-lived, boys were to some extent protected in the first outbreak they experienced, only to be infected later. Revaccination with later strains did not cause the boys to "update" their immunity and, for the individual, the inevitable was only postponed. If a child is going to get influenza at some time, it is probably better for him to get it early in his school career, rather than when he is preparing for important examinations.

One problem identified in considering the cost-effectiveness of vaccination was that only a small proportion of those vaccinated could be expected to benefit. Some were already immune as a result of recent infection and did not respond to vaccine. Of the susceptibles, those who had had no previous experiences of a sub-type did often produce a response sufficient to protect them against subsequent challenge with a "drifted" strain. The best results were obtained in those who had had some experience of a sub-type in the past and whose immunity could be boosted by vaccination.

The advent in 1978 of a "new" sub-type, influenza A H1N1, which had not been in circulation for 20 years, provided an opportunity to study the impact of a strain to which the whole school population was susceptible. It was calculated that 90 per cent of the boys were infected. Fortunately the symptoms were generally not severe; indeed nearly half of those infected did not report any symptoms. This sub-type revisited the school in 1983 and again spread widely. Even those who had been infected in 1978 had an attack rate of about 30 per cent.

The co-operation of the school medical officer and of the boys themselves has made possible a unique study of influenza. This has been extended to other schools to prepare the ground for the assessment of more effective vaccines when these become available.

Current research in collaboration with colleagues at the National Institute for Biological Standards and Control is concerned with small changes in the virus that occur during an outbreak. These studies on the protein chemistry of strains and their reactions to a range of monoclonal antibodies will be related to the previous experience of individuals and their reponse to infection.

PARACETAMOL POISONING – APPLICATION OF MICROBIOLOGY TO THE DEVELOPMENT OF A DIAGNOSTIC KIT

Professor A. Atkinson

Microbial Technology Laboratory, PHLS Centre for Applied Microbiology and Research, Porton Down, Salisbury, Wiltshire SP4 0JG

In 1980, about 43 000 patients aged more than five years were admitted to hospital due to poisoning and the second most common substance used was paracetamol.

In poisoning by this popular "pain-killer", treatment must be given within 12 hours in order to be effective. Failure to do so may result in serious liver damage and sometimes damage to the kidney also. Some of the drugs used in treatment may themselves give rise to unpleasant side-effects, such as rapid heart beat or anorexia. For effective patient management accurate knowledge of blood paracetamol levels is required.

Although technically adequate means of assay are available by specialized reference methods, procedures for use in emergencies are less reliable. This problem was recognized by clinicians and a small collaborative venture to examine the problem was set up between Addenbrooke's Hospital, Cambridge, and the Microbial Technology Laboratory, PHLS Centre for Applied Microbiology and Research (CAMR). It was decided that the specificity offered by an enzymic reaction and the visual advantages offered by a colour change would provide the most robust assay. As no such enzyme was known, a new source was sought.

Initially, a screen of numerous soil samples was undertaken to isolate a bacterium capable of degrading paracetamol. To ensure that degradation did occur, paracetamol was presented to the soil bacteria in a minimal salts medium as the sole source of carbon. A total of three isolates was obtained. Two of these proved unsuitable; the third was used in subsequent assay development. After identification of the isolated bacterium as *Pseudomonas fluorescens*, the biochemistry of paracetamol assimilation was examined. An enzyme (aryl acylamidase) was extracted and purified using a variety of conventional chromatographic techniques. Aryl acylamidase is used to hydrolyse paracetamol, producing *p*-aminophenol and acetate. The major advantage of this enzyme-mediated reation is that it employs gentle hydrolysis, as opposed to the harsh conditions required for hydrolysis by acid. The enzymic reaction is also more specific, having no undesired effects on the conjugates of paracetamol. Reaction of *p*-aminophenol with *o*-cresol in the presence of ammoniacal copper sulphate produces an indophenol dye which can be estimated colorimetrically.

The complete assay has been extensively tested and compares favourably with existing procedures. It is accurate, precise, simple to use, and gives a result in less than 10 minutes. The assay covers both the therapeutic and toxic concentration range. Due to the high specificity of the procedure, it can also be used as a diagnostic test to confirm the presence of the drug. This

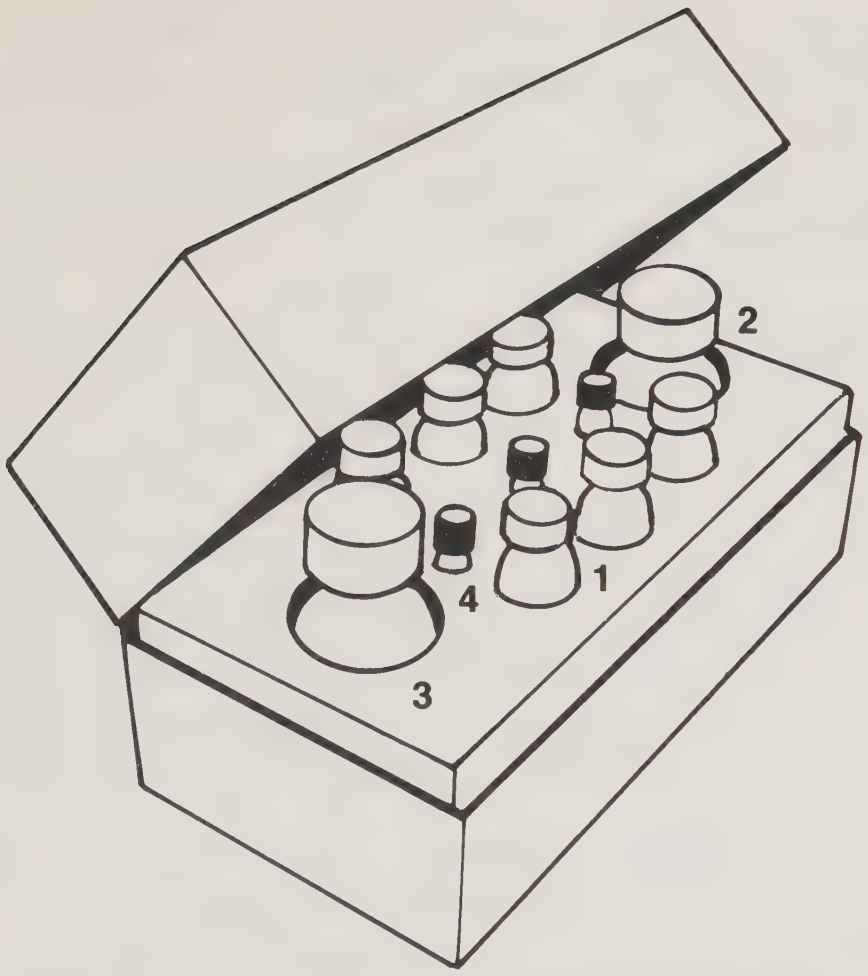

Figure 7 A diagrammatic representation of the design of the diagnostic kit for paracetamol poisoning. *Key*: 1, enzyme reagent (buffered aryl acylamide amidohydrolase); 2, colour reagent A (*o*-cresol in distilled water); 3, colour reagent B (ammoniacal copper sulphate); 4, aqueous standard (paracetamol, 2.0 mmol/l = 302 mg/l).

can be particularly important where an unconscious patient is admitted to hospital. It may also find a wider use for monitoring patients receiving paracetamol whose renal function is abnormal.

The assay system was patented by CAMR and a commercial partner sought to market a diagnostic assay kit based upon this research. An agreement was evenually drawn up and the technology licensed to a newly created British company, Cambridge Life Sciences. The kit was launched on the UK market in November 1982 and was well received. After a year the kit is estimated to have taken approximately 30 per cent of the available market. Users have commented on its clinical usefulness, rapidity and the ease of use afforded by its compact design (Figure 7). In many smaller hospitals it has replaced existing "simple" procedures; in larger hospitals it is used when reference laboratory procedures are not readily available, for example at night. The kit should earn substantial royalties abroad; its launch on the European and American markets is imminent.

In June 1983 the research and development work leading to this diagnostic kit was awarded first prize in the Biotechnology 1983 awards by the British

Laboratory Ware Association. The award was made for innovation in research by a British team, leading to a novel product which had made a significant contribution to the progress of scientific laboratory technology.

OUTBREAK OF *SALMONELLA NAPOLI* INFECTION CAUSED BY CONTAMINATED CHOCOLATE BARS

Mr P. N. Sockett

PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ

In May 1982, three reports of an unusual salmonella serotype, *S. napoli*, were received by the PHLS Communicable Disease Surveillance Centre (CDSC). A further 29 cases were reported in June, most of them in young children living in the south of England. The Division of Enteric Pathogens (DEP) had recorded only 15 human isolations and no non-human isolations in the United Kingdom in the previous 30 years, and as a common source of infection for the 1982 cases seemed likely, an epidemiological investigation was undertaken by CDSC.

Initial enquiries made by telephone and visits suggested several possible vehicles of infection. In mid-July 10 cases from seven families in Colchester and Croydon were interviewed and imported Italian chocolate products were shown to be a common factor: six patients had definitely eaten chocolate bars manufactured by one company and three of the remaining four had possibly eaten the same products.

A preliminary case control study showed strong association between consumption of two types of chocolate-covered bars, called "Rocky Junior" and "Tommy Junior", and gastroenteritis due to *S. napoli*. This evidence and concurrent isolation of the organism from chocolate bars by the PHLS laboratory at Ipswich resulted in a public health warning, issued by the Department of Health and Social Security on 23 July. Wholesale distribution effectively ceased from this date (Figure 8).

Altogether, between May and August 1982, 272 human isolates of *S. napoli* were reported: 202 primary cases, 43 household contacts of cases and 27 symptomless excreters. Of the primary cases over half (118) were children under 15 years and the majority of those over 15 years (60 per cent) were women. Fifty-one of 245 reported cases (21 per cent) were admitted to hospital, 16 had bacteraemia and other individuals had complications including peritonitis, diabetic coma, septic arthritis and ischiorectal abscess. Although the mean duration of stay was 7 days, some cases were still in hospital after 6 weeks. Thirty-two of the 37 adults interviewed were off normal activity for between 8 and 14 days.

S. napoli was isolated from the chocolate bars in 29 laboratories and 107 of 224 (48 per cent) "Rocky" bars and 47 of 146 (32 per cent) "Tommy" bars were positive. Five laboratories demonstrated that the organism was present

in the 3 grams of chocolate covering the bars but not in the cream filling or marzipan base. Estimates of the level of contamination ranged from two to more than 23 organisms per gram of chocolate. Examination of batch numbers showed that bars produced on 11 separate days over a 6 week period in November and December 1981 were contaminated and investigation revealed that the bars were produced on alternate weeks on the same production line.

Importation of the products began in March 1982 and continued until July. Distribution was initially in the south of England, and up to 26 June 80 per cent of cases were in this area. Distribution began in the Midlands in early July and eventually 60 per cent of cases were recorded from this part of the country.

Epidemiological studies by the Instituto Superiore di Sanita in Rome revealed that an outbreak of similar proportions in two regions of northern Italy had taken place between January and June 1982. The incidence of illness in children less than 15 years old in Italy (63 per cent) was very similar to that in the UK (60 per cent). However, the study which took place there after the outbreak had ended showed no association between illness and chocolate consumption.

The outbreak was detected by surveillance of routine laboratory reports of salmonella infections from PHLS and NHS laboratories. Early recog-

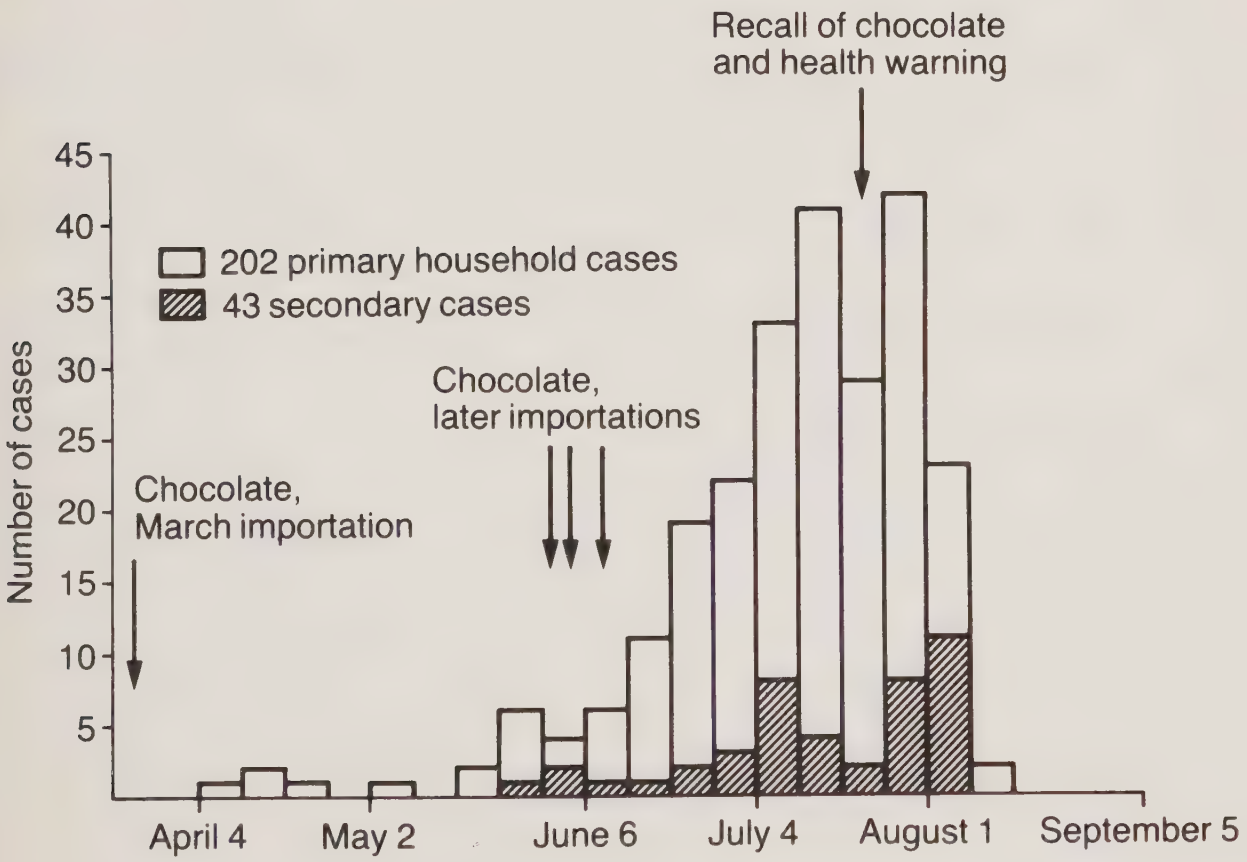

Figure 8 Epidemic curve of 245 cases identified in England and Wales during the 1982 outbreak of *Salmonella napoli*.

nition and investigation rapidly identified the source and 80 per cent of the 3 million bars imported were recalled and destroyed and no new cases were reported within 3 weeks of the recall. Approximately 600 000 bars had been sold, resulting in 245 known cases of illness, including 51 admissions to hospital. However, investigations of other salmonella outbreaks estimate that the ratio of reported to total cases varies between 1 : 30 and 1 : 100. On this reckoning it is likely that about 200 hospital admissions and many thousands of cases were prevented by destroying the remaining 2.4 million bars. It is clear that this investigation, in which there was close co-operation between the Public Health Laboratory Service, hospital laboratories, environmental health departments and the DHSS, prevented much human illness, with a consequent considerable saving of National Health Service resources.

Senior Staff Changes

NEW APPOINTMENTS

Mrs Susan M. Bloomfield	Librarian, Central Public Health Laboratory, 1.11.82
Mr D. S. Broadfield	Personnel Officer, Headquarters Office, 6.9.82
Dr E. Mary Cooke	Consultant Medical Microbiologist, Director, Division of Hospital Infection, Central Public Health Laboratory, 11.10.82
Mr J. M. Harker	Deputy Secretary to the Board, Headquarters Office, 1.2.83
Dr D. N. Hutchinson	Consultant Medical Microbiologist, Director, Preston, 1.10.82
Dr N. F. Lightfoot	Consultant Medical Microbiologist, Taunton, 1.5.82
Dr J. A. Lowes	Consultant Medical Microbiologist, Southampton, 1.6.82
Dr T. Riordan	Consultant Medical Microbiologist, Manchester, 1.9.82
Mr K. M. Saunders	Finance Officer, Headquarters Office, 1.7.82

TRANSFERS

Dr C. Dulake	Consultant Medical Microbiologist, Director, Maidstone, 8.1.83, from Dulwich

RETIREMENTS

Dr Joan M. Boissard	Consultant Medical Microbiologist, Cambridge, 30.9.82
Dr Joan M. B. Edwards	Consultant Medical Microbiologist, Virus Reference Laboratory, Central Public Health Laboratory, 31.3.83
Dr A. L. Furniss	Consultant Medical Microbiologist, Director, Maidstone, 7.1.83
Dr A. D. Macrae	Consultant Medical Microbiologist, Nottingham, 3.8.82
Dr L. Robertson	Consultant Medical Microbiologist, Director, Preston, 7.4.82
Miss Betty Whyte	Librarian, Central Public Health Laboratory, 31.8.82

RESIGNATIONS

Mr A. J. Haggar	Finance Officer, Headquarters Office, 1.7.82
Mr P. Murphy	Deputy Secretary to the Board, Headquarters Office, 15.9.82
Mr P. P. Taylor	Personnel Officer, Headquarters Office, 31.8.82

Honours, Awards and External Offices

Professor A. Atkinson	British Laboratory Ware Association Award for development of a diagnostic kit making use of a paracetamol-degrading enzyme (in association with Dr Scawen)
Dr A. Baskerville	Executive Editor, *Laboratory Animals*
Mr R. A. Brooks	Chairman, Medical Laboratory Technicians Board, Council for Professions Supplementary to Medicine, January 1983
Mr C. H. Collins	Editor, *Journal of Applied Bacteriology*
Dr C. H. L. Howells	Vice President, Association of Clinical Pathologists
Dr P. A. Jenkins	President, Welsh Microbiological Association
Mrs P. Kean	Winner (1982), J. D. Atkinson Memorial Prize
Professor J. R. Pattison	Editor, *Journal of Hygiene*
Dr B. Rowe	Awarded Territorial Decoration (TD)
Dr M. D. Scawen	British Laboratory Ware Association Award for development of a diagnostic kit making use of a paracetamol-degrading enzyme (in association with Professor Atkinson)
Professor P. M. Sutton	Visiting Professor, Department of Biochemical Pathology, University College, University of London

Senior PHLS Staff

The following lists are accurate as at 31 December 1983.

HEADQUARTERS OFFICE

61 Colindale Avenue, London NW9 5EQ
Tel: 01-200 1295

Dr J. E. M. Whitehead	Director of the Service
Dr Joan R. Davies	Deputy Director of the Service (part-time)
Dr P. D. Meers	Deputy Director of the Service
Dr R. A. Bassett	Assistant Director of the Service
Mr R. B. Paget	Secretary to the Board
Mr J. M. Harker	Deputy Secretary to the Board
Mr K. M. Saunders	Finance Officer
Mrs Susan D. Chaney	Deputy Finance Officer
Mr D. S. Broadfield	Personnel Officer
Mr M. Whitney	New Colindale Project Manager
Mrs Christine R. Shipp	Acting Manager, PHLS Computer Services
Mr M. R. Turner	New Colindale Commissioning Officer
Mr J. B. Towell	Supplies Officer

CENTRAL PUBLIC HEALTH LABORATORY

Colindale Avenue, London NW9 5HT
Tel: 01-205 7041

Professor A. A. Glynn	Director
Mr V. Fuller	Administrator

Mrs Susan M. Bloomfield	Librarian
Dr B. Rowe	Director, Division of Enteric Pathogens
Dr E. Mary Cooke	Director, Division of Hospital Infection
Dr P. S. Gardner	Director, Division of Microbiological Reagents and Quality Control, *and* Deputy Director, CPHL
Dr Sheila Polakoff	Acting Director, Epidemiological Research Laboratory
Dr R. J. Gilbert	Director, Food Hygiene Laboratory
Dr L. R. Hill	Curator, National Collection of Type Cultures
Dr Marguerite S. Pereira	Director, Virus Reference Laboratory

PHLS CENTRE FOR APPLIED MICROBIOLOGY AND RESEARCH

Porton Down, Salisbury, Wiltshire SP4 0JG
Tel: 0980-610391

Dr P. M. Sutton	Director
Mr P. Holmes	Deputy Director
Mr I. R. Ingrey-Counter	Administrator
Mr D. Kitching	Deputy Administrator
Dr M. J. Hill	Director, Bacterial Metabolism Research Laboratory
Professor T. Atkinson	Director, Microbial Technology Laboratory
Dr A. E. Wright	Director, Environmental Microbiology and Safety Reference Laboratory
Dr P. J. Greenaway	Director, Molecular Genetics Laboratory
Professor D. C. Ellwood	Director, Pathogenic Microbes Research Laboratory
Dr E. T. W. Bowen	Acting Director, Special Pathogens Reference Laboratory
Dr H. E. Wade	Director, Therapeutic Products Laboratory

Professor J. Melling	Director, Vaccine Research and Production Laboratory
Dr A. Baskerville	Director, Experimental Pathology Laboratory

PHLS COMMUNICABLE DISEASE SURVEILLANCE CENTRE

61 Colindale Avenue, London NW9 5EQ
Tel: 01-200 6868

Dr N. S. Galbraith	Director
Dr Susan E. J. Young	Deputy Director
Mr A. A. Collins	Administrator

OTHER REFERENCE LABORATORIES AND UNITS

Dr A. T. Willis	Director, PHLS Anaerobe Reference Unit, PHLS Laboratory, Luton
Dr Joan R. Davies	Director, PHLS Influenza Research Unit, PHLS Laboratory, Guildford
Dr Sheena M. Waitkins	Director, PHLS Leptospira Reference Unit, PHLS Laboratory, Hereford
Professor D. J. Bradley	Co-Director, PHLS Malaria Reference Laboratory, London School of Hygiene and Tropical Medicine
Professor W. Peters	Co-Director, PHLS Malaria Reference Laboratory, London School of Hygiene and Tropical Medicine
Dr P. A. Jenkins	Director, PHLS Mycobacterium Reference Unit, PHLS Laboratory, Cardiff
Professor D. W. R. Mackenzie	Director, PHLS Mycological Reference Laboratory, London School of Hygiene and Tropical Medicine
Dr B. E. Andrews	Director, PHLS Mycoplasma Reference Laboratory, PHLS Laboratory, Norwich
Dr Nafra A. Johnston	Acting Director, PHLS Venereal Diseases Reference Laboratory, London Hospital Research Laboratories (to 30.9.83)

REGIONAL LABORATORIES

Addresses and telephone numbers of PHLS regional laboratories are listed in relevant telephone directories.

Dr J. G. P. Hutchison	Director, PHLS Laboratory, Birmingham
Dr A. E. Jephcott	Director, PHLS Laboratory, Bristol
Dr C. E. D. Taylor	Director, PHLS Laboratory, Cambridge
Dr C. H. L. Howells	Director, PHLS Laboratory, Cardiff
Dr R. N. Peel	Director Designate, PHLS Laboratory, Leeds
Dr G. C. Turner	Director, PHLS Laboratory, Liverpool
Dr D. M. Jones	Director, PHLS Laboratory, Manchester
Dr J. B. Selkon	Director, PHLS Laboratory, Newcastle upon Tyne *and* Director, PHLS Laboratory, Oxford
Dr O. A. Okubadejo	Director, PHLS Laboratory, Portsmouth
Dr B. W. Barton	Director, PHLS Laboratory, Sheffield

AREA LABORATORIES

Addresses and telephone numbers of PHLS area laboratories are listed in relevant telephone directories.

Dr P. G. Mann	Director, PHLS Laboratory, Bath
Dr B. T. Thom	Director, PHLS Laboratory, Brighton
Dr D. G. Davies	Director, PHLS Laboratory, Carlisle
Dr H. D. S. Morgan	Director, PHLS Laboratory, Carmarthen
Dr R. Pilsworth	Director, PHLS Laboratory, Chelmsford
Dr Pauline M. Poole	Director, PHLS Laboratory, Chester
Dr P. R. Mortimer	Director, PHLS Laboratory, Coventry
Dr Patricia Gill	Director, PHLS Laboratory, Dorchester
Dr D. R. Gamble	Director, PHLS Laboratory, Epsom
Dr R. J. C. Hart	Director, PHLS Laboratory, Exeter
Dr K. A. V. Cartwright	Director, PHLS Laboratory, Gloucester
Professor R. Y. Cartwright	Director, PHLS Laboratory, Guildford

Dr I. R. Ferguson	Director, PHLS Laboratory, Hereford
Dr S. L. Mawer	Director, PHLS Laboratory, Hull
Dr P. H. Jones	Director, PHLS Laboratory, Ipswich
Dr C. J. Mitchell	Director, PHLS Laboratory, Leicester
Dr J. G. Wallace	Director, PHLS Laboratory, Lincoln
Dr D. A. McSwiggan	Director, PHLS Laboratory, Central Middlesex Hospital, London
Dr Anne H. C. Uttley	Director, PHLS Laboratory, Dulwich, London
Dr D. G. Fleck	Director, PHLS Laboratory, Tooting, London
Dr B. Chattopadhyay	Director, PHLS Laboratory, Whipps Cross, London
Dr A. T. Willis	Director, PHLS Laboratory, Luton
Dr C. Dulake	Director, PHLS Laboratory, Maidstone *and* Director Designate, PHLS Laboratory, Ashford
Dr E. McKay-Ferguson	Director, PHLS Laboratory, Middlesbrough
Dr W. Shepherd	Director, PHLS Laboratory, Norwich
Dr M. J. Lewis	Director, PHLS Laboratory, Nottingham
Dr R. S. Jobanputra	Director, PHLS Laboratory, Peterborough
Dr P. J. Wilkinson	Director, PHLS Laboratory, Plymouth
Dr W. L. Hooper	Director, PHLS Laboratory, Poole
Dr D. N. Hutchinson	Director, PHLS Laboratory, Preston
Dr J. V. Dadswell	Director, PHLS Laboratory, Reading
Dr F. B. Jackson	Director, PHLS Laboratory, Rhyl
Dr Sharon Patrick	Director, PHLS Laboratory, Salisbury
Dr C. A. Morris	Director, PHLS Laboratory, Shrewsbury
Dr A. D. Pearson	Director, PHLS Laboratory, Southampton
Dr J. Gray	Director, PHLS Laboratory, Stoke-on-Trent

Dr W. Kwantes	Director, PHLS Laboratory, Swansea
Dr J. V. S. Pether	Director, PHLS Laboratory, Taunton
Dr W. A. Telfer Brunton	Director, PHLS Laboratory, Truro
Dr M. T. Moulsdale	Director, PHLS Laboratory, Watford
Dr R. G. Thompson	Director, PHLS Laboratory, Wolverhampton

Principal Committees

Chairmen and Secretaries of committees are given as at 31 December 1983.

COMMITTEES APPOINTED BY THE BOARD

Finance Committee	*Chairman*: Dr C. E. Gordon Smith *Secretary*: Mr K. M. Saunders
Capital Projects Committee	*Chairman*: Mr C. C. Stevens *Secretary*: Mr J. M. Harker
Steering Committee for the Communicable Disease Surveillance Centre	*Chairman*: Dr J. E. M. Whitehead *Secretary*: Dr Susan E. J. Young
Steering Committee on External Quality Assessment in Microbiology	*Chairman*: Dr Joan R. Davies *Secretary*: Dr P. R. Mortimer
Steering Committee on Income Generating Activities	*Chairman*: Professor M. H. Richmond *Secretaries*: Dr R. A. Bassett and Mr J. M. Harker
Ethical Committee	*Chairman*: Professor Rosalinde Hurley *Secretary*: Professor A. A. Glynn

COMMITTEES APPOINTED BY THE DIRECTORS' MEETING

Standing Advisory Committee on Electron Microscopy	*Chairman*: Dr T. H. Flewett *Secretary*: Dr Anne M. Field
Standing Advisory Committee on Influenza	*Chairman*: Dr R. J. C. Hart *Secretary*: Dr C. A. Morris
Standing Advisory Committee on Laboratory Safety	*Chairman*: Dr A. E. Wright *Secretary*: Dr J. V. S. Pether
PHLS Publications Editorial Committee	*Chairman*: Dr R. J. C. Hart *Secretary*: Mr E. M. D. Scott

PHLS Publications Management Committee	*Chairman and Secretary*: Mr J. M. Harker
Standing Advisory Committee on Serological Reagents	*Chairman*: Dr Joan R. Davies *Secretary*: Dr P. S. Gardner
Standing Advisory Committee on Sexually Transmitted Diseases	*Chairman*: Dr G. C. Turner

SUBCOMMITTEES AND WORKING PARTIES

PHLS Library Policy Subcommittee	*Chairman*: Dr R. A. Bassett *Secretary*: Mrs Susan M. Bloomfield
Standing Subcommittee on Bacteriological Examination of Water Supplies	*Chairman and Secretary*: Dr G. I. Barrow
Subcommittee on Hepatitis	*Chairman*: Dr J. Craske *Secretary*: Dr Sheila Polakoff
Subcommittee on Salmonellas	*Chairman*: Dr J. G. Cruickshank *Secretary*: Dr S. L. Mawer
Working Party on Human Infections by Group B Streptococci	*Convenor*: Dr B. T. Thom *Secretary*: Dr R. T. Mayon-White
Working Party on Streptococcal Infection in Abattoir Workers	*Chairman*: Dr C. A. Morris *Secretary*: Dr H. W. K. Fell
Working Party on Campylobacter Infections	*Chairman*: Dr M. B. Skirrow
Zoonoses Consultative Panel	*PHLS representatives*: Director of the Service (or Deputy), Dr G. I. Barrow, Professor R. Y. Cartwright, Dr B. Rowe

Accounts of the PHLS Board 1982/3

The tables on the following pages provide a summary of the accounts of the PHLS Board for 1982/3. These tables represent an abbreviated statement of transactions for 1982/3, which has yet to be subjected to formal government audit.

Table 5 Accounts of receipts and payments for the year ended 31 March 1983

Receipts				Payments				
Prior year ended 31 March 1982				Prior year ended 31 March 1982		Salaries, including superannuation contributions	Other expenditure	Total
£		£	£	£		£	£	£
63 102	Balance 1 April 1982		250 936		Current:			
26 139 117	Department of Health and Social Security Advances		29 937 947					
1 356 673	Welsh Office Advances		1 402 740	1 125 656	Administration	544 206	540 653	1 084 859
				5 020 167	Central and special laboratories	3 489 619	1 493 387	4 983 006
	Public Health Laboratory Service laboratories				Centre for Applied			
	Grants from other organizations			5 392 315	Microbiology and Research	3 090 912	2 551 314	5 642 226
				15 872 538	Constituent laboratories	12 534 011	3 884 314	16 418 325
33 059	World Health Organization	25 162						
108 486	Medical Research Council	93 333			Central Supply Services			
83 022	Cancer Research Campaign	59 725						
78 372	Other bodies	77 371	255 591		Excess of purchases over			
				161 585	issues	—	80 251	80 251
	Proceeds of sales, fees, etc:			202 077	Central services	147 072	239 847	386 919
33 082	Sales of cultures and reagents	41 326			Total Current Payments	19 805 820	8 789 766	28 595 586
147 120	Central Supply Services to other bodies	198 493						
81	Laboratory service fees							
2 258 035	Rechargeable salaries and services	2 510 769						
26 625	Bench fees	33 420						
26 326	Other receipts	34 216	2 818 224		Capital			
	Centre for Applied Microbiology and Research			4 608 717	New buildings and associated equipment			8 561 869
	Grants from other organizations							
33 677	Medical Research Council	83 217						
29 303	Cancer Research Campaign	128 779		250 936	Balance 31 March 1983			201 415
132 079	Other bodies	185 069	397 065					
	Proceeds of sales, fees, etc:							
948 538	Sales of products etc.	1 098 457						
912 844	Other receipts	864 057	1 962 514					
224 450	Capital payments recharged							
	PHLS	18 492						
	CAMR	315 361	333 853					
£32 633 991			£37 358 870	£32 633 991				£37 358 870

The cost of this service, administered by the Public Health Laboratory Service Board, was borne on Health and Personal Social Services, England, Class XI, Vote 1, and for the Welsh laboratories on Class XVI, Vote 1.

Statement of losses, etc. Cases of loss or compensation totalled £4468.50: 33 compensation payments, £1115.06; two losses due to theft, £91.26; three personal injury settlements, £3105.00; and accumulated stores stock write-off, £157.18.

Table 6 Account of special funds for the year ended 31 March 1983

Receipts		Payments	
	£		£
Balance at 1 April 1982	15 580	Headquarters Fund	100
Donations	588	CPHL Rabies Account	153
Bank interest	1 016	Ascorbate Fund	9 775
		Balance at 31 March 1983	7 156
	17 184		17 184